

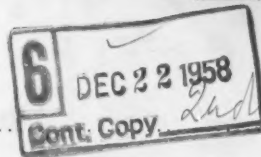
Sci Bible

12/31/58

# SCIENCE

19 December 1958

Volume 128, Number 333



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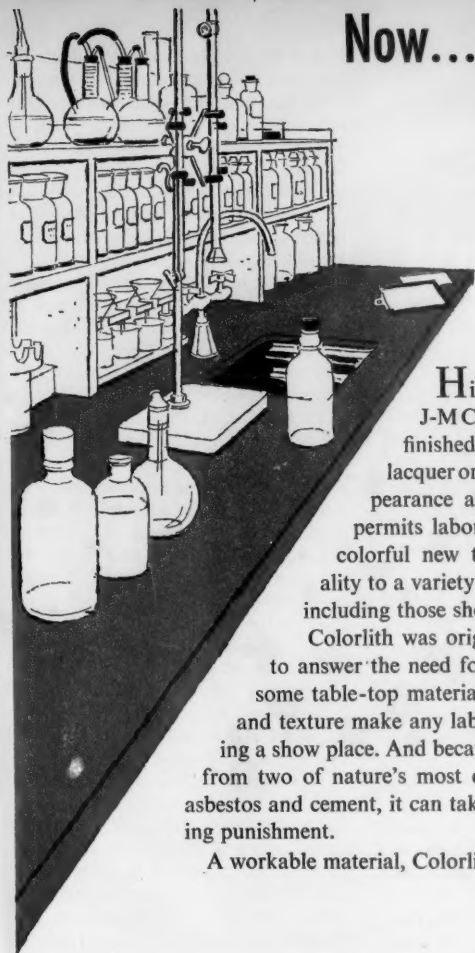
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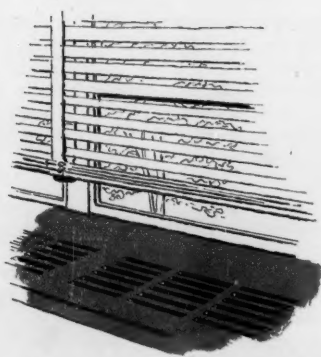
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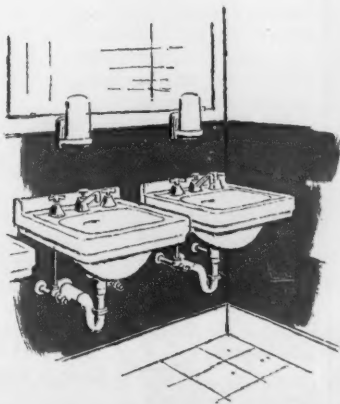
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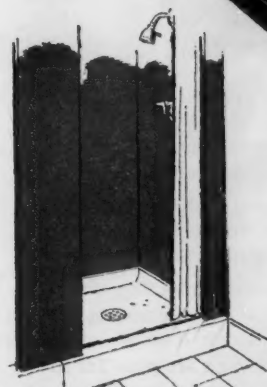
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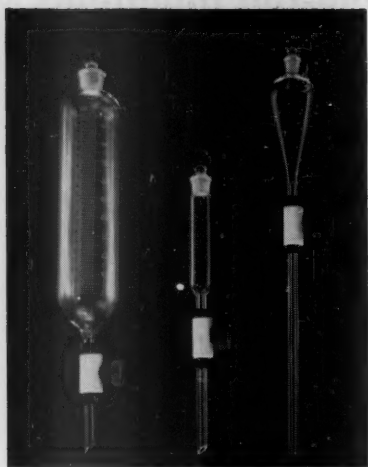
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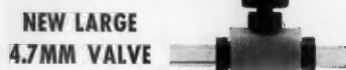
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## Letters

### Initial Modesty

Authors "who believe that the use of *I* or *we* is immodest" were gently chided for their false modesty in the lead editorial, "Passive voice," in *Science* for 22 March 1957 [125, 529 (1957)]. But authors who prefer not to write in the first person are much more honest than those, like the author of the editorial in question, who write in the first person without signing their names.

An editorial, report, or article whose author is identified only by initials has an anomalous status. Does it represent the view or opinion of the editorial board, as competently expressed by one member? Or does the use of initials imply a disclaimer by the board as a whole, so that only the owner of the initials is to be held responsible?

If cryptic initials are used only for internal identification, they should be much less obtrusive—perhaps in 6-point type, or in the form of a code number or of initials run together without periods, even in reverse order. As used, full size, in *Science*, initials usually can be matched up with one of the names in the masthead, so they offer little anonymity. The editorial in question was signed "R.V.O."—presumably Robert V. Ormes, a member of the editorial staff. Was Ormes so ashamed of his editorial that he did not wish his full name attached to it?

(Perhaps he should be ashamed. For an essay on grammatical purity, its own purity leaves something to be desired. I was particularly set on edge by the sentence: "In the editorial office we still see gerunds and participles used in this manner, and it is discouraging." Is the manner discouraging?)

In addition to making an unclaimed orphan out of an editorial or note, the use of initials, rather than an honest name, imposes an unwarranted burden on the poor bibliographer. Forever more, this editorial must be listed as: "R(ober?) V. O(rmes?): Passive Voice," or "R.V.O. (Robert V. Ormes?): Passive Voice." Bibliographers should not be forced to pay thus for an unsure author's false modesty.

ARNOLD COURT

Berkeley, California

### Radiation Hazards

In the article entitled, "Mice, men, and fallout" [*Science* 128, 637 (1958)], M. P. Finkel presents some interesting results regarding the effects of low doses of Sr<sup>90</sup> on mammalian life expectancy and incidence of certain tumors. However, in discussing these results, the author draws far-reaching conclusions relating to the danger to man (or rather

lack of it) from present Sr<sup>90</sup> fallout. The concluding sentence states, "the present contamination with strontium-90 from fallout is . . . extremely unlikely to induce even one bone tumor or one case of leukemia." I would like to raise the following points with regard to this conclusion.

1) In the data presented, the uncertainty was such that a 7-percent shortening of life span in an experimental group did not represent a statistically significant deviation from the control, nor did a threefold increase in the incidence of osteogenic sarcomas. Yet the above statement refers to effects on the world's population which would amount to a small fraction of 1 percent.

2) No statistically justifiable extrapolation for determination of "threshold doses," or even demonstration that there is a threshold different from zero, seems possible from the data as presented. In fact, these data appear to indicate that the experimental design used is inadequate for this purpose.

3) At the present time, sober and accurate evaluations of the effects of chronic low-level irradiation of human populations, from internal and external radioisotopes, are essential for the formulation of safe and wise national and international policies regarding the testing of nuclear weapons and the development of nuclear power. It is unfortunate that at this time a statement such as that quoted above is published with the implication that it is based on experimental evidence, when actually it appears to be without objective, logical support. Unfounded statements *minimizing* radiation hazards can be especially harmful if they turn out later to have been false.

A more appropriate conclusion from the data would seem to be that drawn by Austin M. Brues from a discussion of other data relating to carcinogenesis [*Science* 128, 693 (1958)]—namely, that a linear dose-effect relation is less probable than a nonlinear relation, and that a threshold *might* occur.

CARL MOOS

College of Medicine,  
University of Illinois, Chicago

I should like to comment on the article by Miriam P. Finkel. First of all, it is difficult to tell whether this article should be considered as an editorial or as a strictly scientific paper. If the latter is the case, I should like to strenuously object to the opening paragraph, which in a back-handed kind of way casts disrepute on some of the most eminent scientists of our time who have been concerned with the effects of fallout on human beings.

Aside from this, I particularly wish to criticize some of the scientific conclusions. The type of effect that one is looking for with respect to the action of fallout on man is such that it has been predicted that several tens of thousands

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of individuals may develop tumors or leukemia. If the entire population of the world is considered, then only one individual in a few hundred thousand might be expected to show this damage, if the magnitude of the effect is what has been predicted. I do not see, therefore, how the figures given in Table 1 of Finkel's article are adequate to enable one to draw the conclusion that there will be no effect of the above-mentioned magnitude. At the lowest level of radiation used (group number 12 of Table 1), it seems to me, the number of animals used should have been approximately 200,000 instead of 150 in order to establish an effect of the magnitude we are seeking. Even with 200,000 animals it might be expected that only one mouse would develop a tumor as the aftermath of the radiation, and therefore the number utilized should be many times greater than 200,000 to establish a statistical significance of the effect at the low levels. In view of this I think the final sentence in the conclusion is extremely unwarranted and is not in accord with an objective scientific appraisal of the data presented.

Although the author points out that there are considerable differences to be expected in the response to radiation of a mouse and of man, I think this point should have been further stressed, particularly in view of the conclusion in the final sentence. One very obvious great difference is the fact that the mouse cells are exposed to the radiation for a period of not more than approximately 2 years, whereas human cells may be exposed to the radiation for a period of 60 to 70 years, with much more far-reaching consequences possibly accruing in the latter case.

I feel that the great publicity given to the article in question in the newspapers has given perhaps an erroneous viewpoint to many laymen who are not familiar with some of the imponderables involved.

JAY S. ROTH

Department of Biological Chemistry,  
Hahnemann Medical College and  
Hospital, Philadelphia, Pennsylvania

The article by Miriam P. Finkel of Argonne National Laboratory propounds very sweeping conclusions on the lack of danger from small doses of ionizing radiations, and particularly from strontium-90 fallout. An examination of the assumptions upon which these conclusions rest is called for. The chief of these is that the main danger of radiations in man's environment lies in their effects on the individuals exposed. The author states (page 637): "At lower levels [of radiation], tumor induction and shortening of life are the major signs of damage." This leads her to restrict her discussion of the evidence as follows: "The most useful criteria of radiation damage to the mammalian organism as a whole

are decrease in life span and increase in incidence of certain tumors." Although she states that "these studies are concerned with the effects upon the exposed generation only," the article shows no sign whatever that the author is aware of the fundamental distinction between somatic and germinal radiation damage.

The undoubted fact that high-energy radiations induce mutations in germ cells would seem to be sufficient reason for at least using caution in discussing a question of such importance as the radiation damage to human populations. The data presented have obviously no bearing on the problem of direct proportionality between the radiation exposure and the number of germinal mutations induced. The question of linearity of response of somatic cells to radiation is treated in a paper by A. M. Brues, from the Argonne Laboratory, in the issue of *Science* following that in which Finkel's paper appeared [128, 693 (1958)]. The conclusion reached is that there is no evidence of linear relationship between carcinogenesis and the dosage of carcinogens, and that this makes a mutational origin of cancer doubtful. Whether or not this conclusion is accepted, the evidence for it is set forth clearly and examined critically. The same cannot be said for Finkel's presentation, which arbitrarily excludes from consideration the genetic radiation damage.

The neglect of elementary methods of critical examination of evidence leads us to doubt not only Finkel's main conclusion that "the present contamination with strontium-90 from fallout is so very much lower than any of these levels that it is extremely unlikely to induce even one bone tumor or one case of leukemia" but also the rationale on which the work was based. Surely understanding of the effects of radiation on populations of organisms, including man, is not likely to be advanced by willful neglect of one of the well-established effects of radiation.

L. C. DUNN

T. DOBZHANSKY

Department of Zoology, Columbia  
University, New York, New York

Moos' comments are most pertinent to the complicated problem of the potential danger from very low doses of radiation. Since the major assumptions upon which the usual estimations of the human hazard have been based are not supported by animal experimentation, there is no reason to believe that straight lines drawn from the effects of moderate doses to zero effect at zero dose have any meaning. My conclusions have been based upon alternative methods of assessing the human hazard.

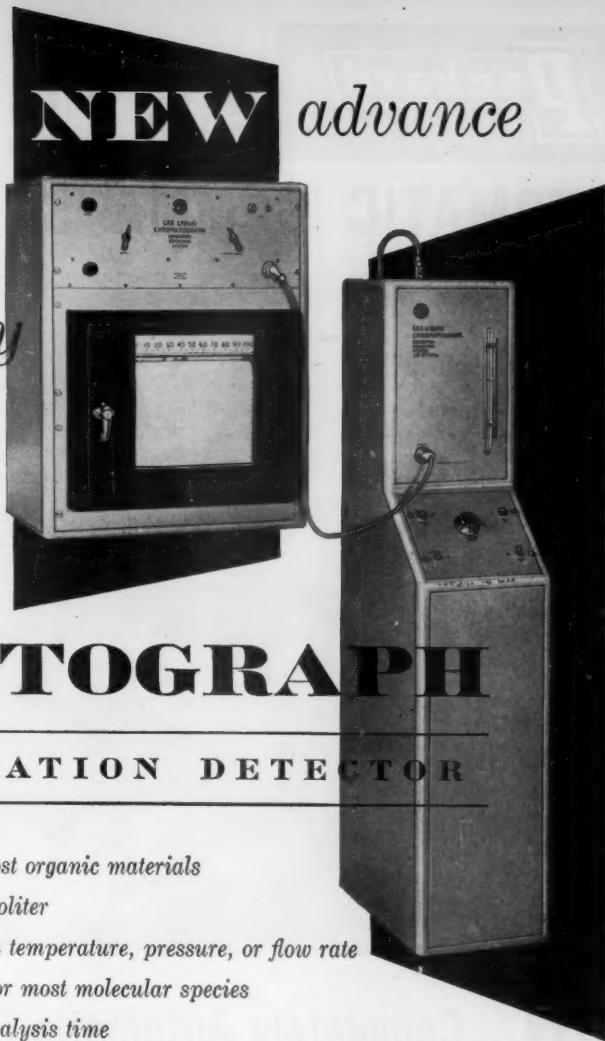
The objection is raised by Moos in point 1 that, in spite of the statistical uncertainties of the values at low levels, statements referring to large populations

(Continued on page 1590)

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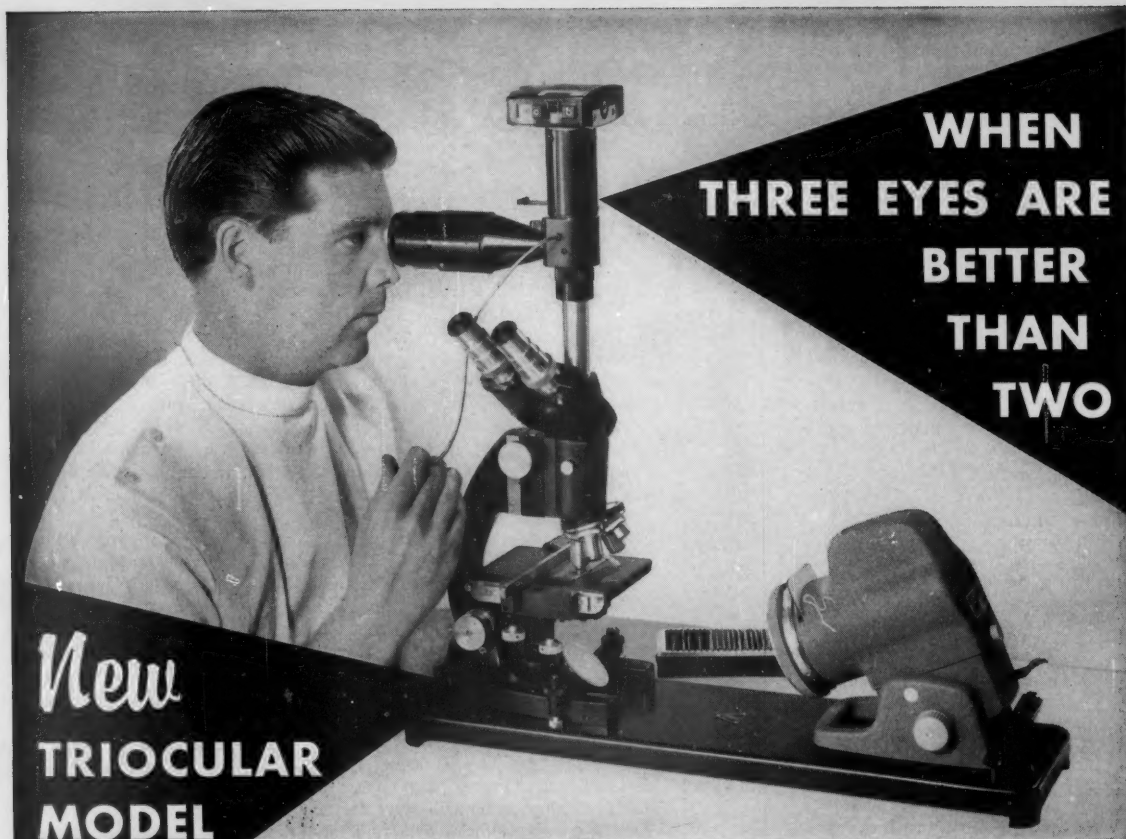
The appointment of Science Officers to serve at several of our embassies (see page 1561, this issue) prompts us to take another look at the role of science in the Department of State. The revival of the science office, which began nearly a year ago with the appointment of Wallace R. Brode as Science Adviser to the Secretary of State [*Science* 127, 175 (24 Jan. 1958)], indicated that the Department recognized the need for a mechanism to ensure that scientific factors would be taken into account in decisions affecting foreign policy and that contact between foreign and American scientists needed to be facilitated.

The general pattern for the organization of the Science Adviser's Office is now clear. At the base is a Washington staff of which the principal officers, in addition to Brode, are as follows: Deputy Science Adviser L. H. Farinholt, who was formerly professor of chemistry and director of the chemical laboratories at Columbia University and science attaché in London in 1954; Assistant Science Adviser Mary E. Corning, physical chemist, who was formerly with the National Bureau of Standards; Raymond L. Zwemer, zoologist, who was for three years chief of the Division of International Cooperation for Scientific Research at UNESCO in Paris; and Assistant to the Science Adviser Walter M. Rudolph, who has been in the science program since its beginnings in 1947.

The Science Officers (who appear to be equivalent to the attachés under the earlier program) will serve for two years and will be backed up by Deputy Science Officers, who will serve similar but overlapping terms to provide for continuity. These officers will be assigned only to certain major and centrally located countries, but they will be expected to keep abreast of developments that bear on foreign policy in neighboring countries. Provision is being made for carrying out similar functions in countries beyond the purview of the Science Officers by the designation of foreign service officers, who have the requisite familiarity with science, to cooperate with the science office.

This is the formal structure. How it will work in practice will depend less upon its table of organization than upon a number of unspecified and informal relations. However favorable the predisposition of the old-line foreign service officers may be to the newly appointed Science Officers, the latter will still have to work out their precise role in the embassies and gain an accepted place. So also, the Science Adviser's office will have to maintain and improve its working relations with such other branches within the Department as the International Cooperation Administration and the Technical Cooperation Administration and with outside agencies such as the National Science Foundation, the National Academy-National Research Council, and the Killian Committee.

The new office has its work cut out for it. Not the least of its tasks will be that of avoiding the gradual attrition that afflicted its predecessor, an attrition which was the more readily brought about by the short-term appointments of scientists; when their terms came to an end, no successors were appointed. The new office has a greater assurance of continuity in that its Washington base is permanently staffed, but the Science Officers are still vulnerable by virtue of their limited terms of appointment. Perhaps the best remedy is to establish career appointments for at least some of the Science Officers, who would thus become scientist-diplomats. A permanent cadre of this kind would give greater continuity of experience and increase the chances that the work would be maintained when the political winds blow cold.—G.DuS.



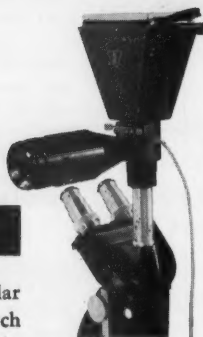
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## CURRENT PROBLEMS IN RESEARCH

### Decomposition of Economic Time Series

Business fluctuations are broken down into seasonal, cyclical, and irregular factors by computers.

Julius Shiskin

During recent years there has been an increased interest in economic developments on the part of the public, particularly during the 1953-54 and 1957-58 recessions. This interest has further stimulated the collection and dissemination of an already imposing array of current economic statistics. A major factor impeding the organization, analysis, and interpretation of these great quantities of data has been the high cost of the required calculations. Electronic computers, however, opened up the possibility of making such calculations quickly and cheaply. An electronic computer method of analyzing business fluctuations prepared at the United States Bureau of the Census in 1954 served to demonstrate the potentialities of computer analysis of economic data. After improvement and extension, this method is now in widespread use in the analysis of economic time series. These series measure, usually at monthly intervals, such things as the production of steel, the number of unemployed, the average price of wheat, stock prices, and the liabilities of business concerns that have failed. Altogether more than 5000 economic time series have been analyzed by the Bureau of the Census for U.S. Government agencies, foreign governments, universities,

and private research organizations. Many business concerns are also using this method to analyze their own performances.

#### Types of Economic Fluctuations

A principal purpose of studying business statistics is to determine the stage of the business cycle at which the economy stands. Such knowledge helps in forecasting subsequent cyclical movements and provides a factual basis for taking steps to moderate the amplitude and scope of the business cycle. It is of critical importance around turning points—for example, failure to recognize a downturn in business may lead to the adoption of policies to curb expansion when a recession is already under way. In using business indicators, however, analysts have been perennially troubled by the difficulty of separating the underlying, more meaningful cyclical movements from other types of fluctuations.

Time series make up the most important raw materials for historical studies of economic events. They are statistical records of economic processes for consecutive and equal periods. They are generally compiled monthly and have been cumulated for long periods. Many are available for each month since the beginning of 1919. A few start prior to

1900; thus, a monthly series on pig iron production covers the period since 1877. These monthly series are supplemented by annual and quarterly series. More recently interest has been turning to weekly series, and about 50 weekly series covering broad economic processes are now compiled currently, for example, on steel production, electric power production, and initial claims for unemployment insurance. Thousands of weekly, monthly, and quarterly economic time series have been compiled by statisticians over the years and are available for study.

For many years economic statisticians have found it useful to consider each economic time series as a composite of cyclical, trend, seasonal, and irregular factors. In the analysis of a given series, the series is decomposed, or broken down, into these parts. (Figure 1 shows the decomposition of an economic time series on private, nonfarm dwellings that were started during the period 1947-1958.) The cycle—usually referred to as the business cycle—consists of short-run movements made up of alternating periods of business expansion and contraction. They last from 3 to 4 years, on the average, though the range extends from 2 to 10 years. The trend is made up of the still-longer-run movements of the series and ordinarily has little effect upon month-to-month movements of economic series. For convenience in short-term forecasting it is often combined with the cyclical factor.

The practice of combining the cyclical and trend factors is followed in this article (1). This should be borne in mind, because sometimes the trend is important, even over short periods—for example, in series showing airline traffic since 1947. The curves used to delineate the cyclical component also show shorter movements that are not generally recognized as cyclical—for example, in a great many economic series there was a rise from July to October 1932 and a decline from the spring to the fall of 1951. Furthermore, the term *cyclical* is used in other sciences, and especially in mathematics, to mean something different—a curve with a recurrent cycle that has a symmetrical pattern, a standard ampli-

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tude, and a fixed period. For these reasons, the use of the word *cyclical* to identify curves in economic studies leaves something to be desired; another word, possibly *systematic* or *oscillatory*, might be preferable if we were starting afresh. But the use of the term *cyclical* to describe alternating periods of business expansion and contraction, with uneven patterns, varying amplitudes, and irregular durations, is so widespread among economists that it would probably be impossible to substitute another term now.

The seasonal factor consists of intra-year movements which are repeated more or less regularly each year. For example, farm income rises steadily each year from early spring to fall and then drops sharply again. Most economic series contain significant seasonal fluctuations, but some (stock prices, for example) contain none. The irregular fluctuations are those that remain after the other types are accounted for. They are occasioned by a wide variety of factors: exceptional events, such as unusual

weather, strikes, unexpected political developments, or the failure of a large business concern, and statistical errors, such as sampling errors, response errors, and errors caused by defective seasonal adjustments.

Irregular, seasonal, and cyclical movements all vary a great deal in magnitude from one series to another. The irregular movements are very large in some series, such as the liabilities of business failures series, but are very small in others, such as the grocery sales series. Similarly, the seasonal factor is quite large in construction and retail trade series but small in many manufacturing series. The cyclical amplitude is considerably larger in new orders and construction series than it is in employment series.

### Role of Computers

The Census Bureau's electronic computers perform arithmetic computations at a very high rate of speed, and their

operations are almost completely automatic. They will select the appropriate one of several series of computations, according to the results of earlier computations. Computers of this class are at their best in performing operations involving long series of sequential or iterative computations on relatively small numbers of original observations. The decomposition of time series fits this requirement very well and, moreover, requires only a small number of input operations (punching and card-to-tape conversion). Although the output of data in the time series decomposition program is large relative to the input, it is easily handled by the Census Bureau's high-speed printers. Recent experience with these computers shows that they make possible the massive application of diagnostic and forecasting techniques that could previously be applied only on a small scale. Computers have also opened up possibilities of types of analysis far beyond the capacity of earlier equipment.

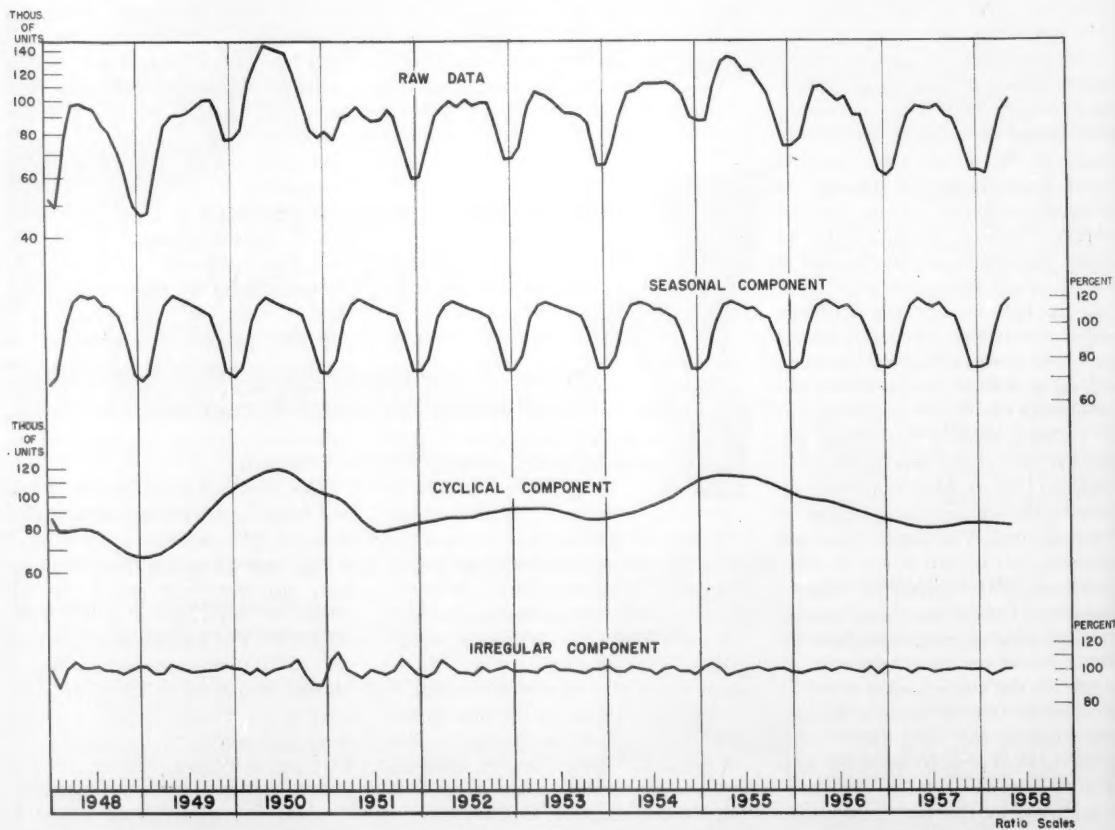


Fig. 1. The Census Bureau time series analysis and adjustment program is designed to separate the seasonal, cyclical, and irregular components of unadjusted economic time series. An example of the raw (unadjusted) data (number of dwelling units started each month) and its derived seasonal, cyclical, and irregular components are represented graphically above. Source of raw data: Bureau of Labor Statistics, U.S. Department of Labor.



The method of time series decomposition developed at the Bureau of the Census eliminates the seasonal factor and irons out the irregular factor so that the cyclical factor stands out more clearly. The application of this method to many economic time series has been helpful in diagnosing current business conditions and forecasting the course of business. Thus, the results were used on a large scale by many Government agencies as an aid in following the course of the 1957-58 recession (2). In addition, studies of the results have revealed some important information about the relations among the components of aggregate economic change. For example, they have shown that in most economic time series both the seasonal and irregular factors dominate the month-to-month movements of the underlying, more meaningful cyclical factor; on the other hand, cyclical movements dominate comparisons made over longer spans, usually three months.

The method used, the tests to which it has been put, and some of the new knowledge yielded by its application are described more fully below. While this work has already been fruitful, this article should be considered primarily as an illustration of the new potentialities in economic research made possible by the advent of the electronic computer.

### Seasonal Adjustments

An adaptation of a widely used method of measuring seasonal variations (the ratio-to-moving-average method) was programmed for the Census Bureau's electronic computers. There were three principal reasons for selecting this method, rather than some other: (i) It had been thoroughly tested in the past and had proved satisfactory for a large variety of economic series; (ii) it permits checking and analysis at each of the many stages in the seasonal adjustment process; and (iii) it had been almost universally accepted by economists and business analysts, who are the chief users of seasonally adjusted data. It is possible that equally good, or even better, results could have been obtained had we started with another method—for example, a regression method or perhaps the link-relative method—and expanded and developed it in a similar way. The development and testing of alternative methods and comparisons with the present method might also add significantly to our knowledge of economic time series analysis.

The first step in the ratio-to-moving-average method is to compute a 12-month moving average—that is, a series of averages for successive 12-month periods (January to December, February to January, March to February, and so on). These annual averages eliminate the seasonal fluctuations and trace out, approximately, a "trend-cycle curve." Division of the raw data by this moving average yields a series of seasonal-irregular ratios. Since both the raw data and the moving average contain the trend-cycle component, it is canceled out (approximately) by division, leaving only the seasonal and irregular components. Estimates of the seasonal adjustment factors are then secured by averaging the seasonal-irregular ratios for successive Januaries, successive Februaries, and so on, in such a way that the irregular factor will be largely canceled out in the averaging process. Finally, the seasonal variations are eliminated from the original observations by dividing these observations by the seasonal adjustment factors. The resulting (seasonally adjusted) series contain the trend, cycle, and irregular factors, but not the seasonal factor.

The adaptation of the ratio-to-moving-average method programmed at the Census Bureau takes advantage of the electronic computer's high-speed, low-cost computations; it utilizes more powerful and refined techniques than clerical methods widely used in the past, so it is likely to produce satisfactory results more frequently. It also produces more information about each series—information that can be used for checking the adequacy of the results, for forecasting seasonal and other movements, and for other purposes. The principal features of the method (3) are summarized below, not with the expectation that the reader will follow them in detail, but to indicate the power and generality of the new method, as well as its limitations.

The electronic computer first computes a preliminary seasonally adjusted series and then goes on to refine it. It utilizes a complex graduation formula—a weighted 15-month moving average applied to the preliminary adjusted series—to obtain the estimate of the trend-cycle curve. This average provides a smoother and more flexible curve than the simple 12-month moving average. A control-chart procedure is employed to identify extreme seasonal-irregular ratios, and the weight of these extreme ratios is systematically reduced in the subsequent computations. Weighted moving averages of the seasonal-irregular ratios for each

month are employed to obtain a set of moving seasonal adjustment factors. A measure of the irregular component of each series is used to determine which of two moving averages to fit to the seasonal-irregular ratios. If the irregular component is relatively small, the machine selects a three-term moving average of a three-term moving average; if the irregular component is relatively large, it selects a three-term moving average of a five-term moving average for greater smoothing. Changing trends are taken into account in calculating seasonal adjustment factors for the full period of the series, including the first and last few years. For each month an average of the seasonal-irregular ratios for the last two years available is taken as the estimated value of each of the ratios for the two or three additional years required for the computations. These estimates provide the full amount of data required to compute the seasonal factors for the end years of the series. A similar procedure is used to obtain missing values for the beginning years of series and for computing the beginnings and ends of the trend-cycle curve.

### Measures of Cyclical-Trend and Irregular Factors

After the program computes seasonal factors—that is, a series estimating the seasonal component of the aggregate series and a seasonally adjusted series—it calculates a curve estimating the cyclical and trend factors in combination. This is accomplished by taking a weighted 15-term moving average of the final seasonally adjusted series. Finally, an irregular series is obtained by dividing the seasonally adjusted series by the cycle-trend curve. Thus, the time series representing the original observations is broken down into three separate series representing the seasonal, cyclical-trend, and irregular components of the aggregate series (see Fig. 1).

A group of summary measures of the seasonal, cyclical, and irregular components and the relations among them are also computed. The average monthly amplitude of the seasonal factor,  $\bar{S}$ , is obtained by averaging the month-to-month percentage changes in the seasonal factor curve without regard to sign. Similarly, the average monthly amplitude of the cyclical factor,  $\bar{C}$ , is obtained by averaging the month-to-month percentage changes in a weighted 15-month moving average of the seasonally adjusted series without regard to sign.

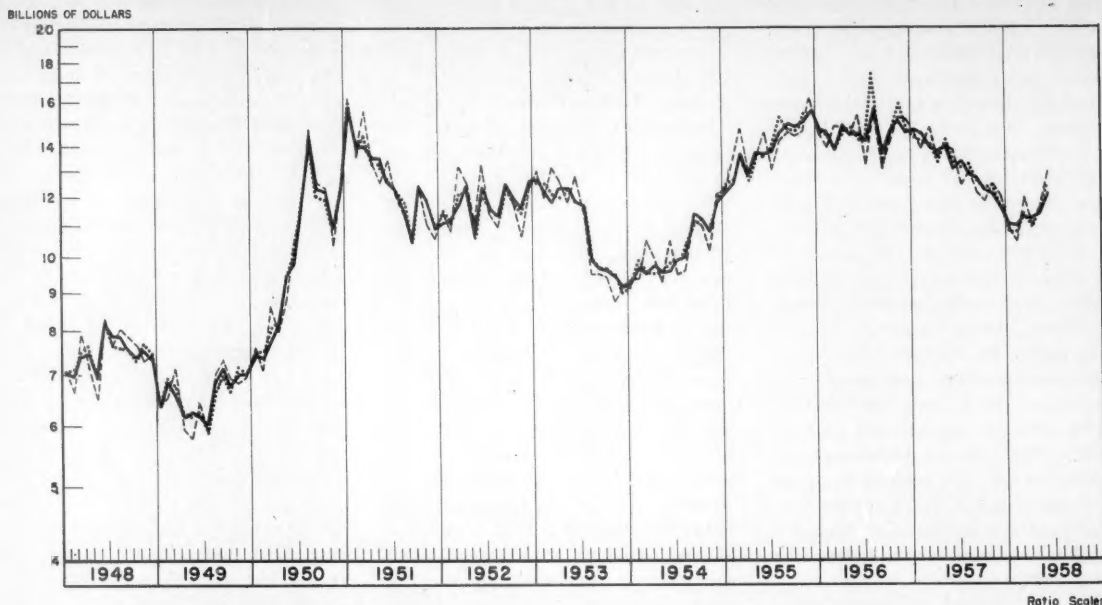


Fig. 2. A variety of manual methods of seasonal adjustment have been in use for many years. This chart shows an unadjusted time series (original observations for manufacturers' new orders of durable goods) (dash line) and compares seasonal adjustments resulting from the computer method (solid line) described in this article and a typical manual method (dotted line). Many such charts for other series have been prepared and show about the same kind of similarities and differences. Source of original observations and manually seasonally adjusted data: Office of Business Economics, U.S. Department of Commerce.

Finally, the average amplitude of the irregular factor,  $\bar{I}$ , is computed by averaging the monthly percentage changes in the ratio of the seasonally adjusted series to the cyclical curve without regard to sign. The machine then uses these measures to compute various ratios of these amplitudes—for example, the ratio of the average amplitude of the irregular factor to the average amplitude of the cyclical factor.

Ratios of the average amplitudes of the irregular to the cyclical factors are computed for 1-, 2-, 3-month, and longer spans (up to 6 months). For the 1-month span the computation is based on the percentage changes for the periods January to February, February to March, and so on; for the 2-month span the percentage changes are computed for the periods January to March, February to April, and so on. Tests show that the magnitude of the irregular amplitude remains about the same, regardless of the span, while the cyclical amplitude cumulates as the span increases. The number of months required for the irregular-cyclical ratio to fall below unity may, therefore, be taken as an index of the months required for the cyclical factor to dominate the irregular factor. This index is identified by the symbol MCD ("months for cyclical dominance");

thus, MCD is 3 for manufacturers' new orders of durable goods and 1 for the index of industrial production. This indicates that comparisons of the industrial production indexes for consecutive months usually show significant economic changes, but that comparisons in manufacturers' new orders usually show significant economic changes only over 3-month or longer spans. The MCD index has proved to be one of the most useful measures yielded by the electronic computer program.

Since the first differences of simple moving totals are equivalent to differences between figures for months separated by an interval equal to the period of the moving average, it follows that a moving average of a seasonally adjusted series calculated for a period equal to MCD would show primarily changes in the cyclical factor. A moving average of this period is automatically computed in the program.

#### Tests of the Electronic Computer Method

Many tests of the accuracy of the time series decomposition method described above have now been made; the two most important are described here (4). A

comparison was made of the seasonal adjustments determined by electronic computer with some of the adjustments prepared clerically at the National Bureau of Economic Research, the Office of Business Economics of the Department of Commerce, and the Department of Agriculture. The National Bureau of Economic Research adjustments used in this test employ stable seasonal factors, with two short periods selected for each series; the Office of Business Economics and the Department of Agriculture employ changing seasonal adjustment factors for the series selected. The results for one of these series, manufacturers' new orders of durable goods, are shown in Fig. 2 (5).

Figure 2 shows that the differences in the results are small. Where they occur, the computer method usually yields the smoother seasonally adjusted series, although this does not necessarily mean that the series is better. It is clear, however, from these and other comparisons, that the computer method can ordinarily be counted upon to yield a seasonal adjustment of as good quality as the best manual methods. Furthermore, this method seems to be versatile enough to make stable and moving adjustments about equally well, though it will not handle abrupt (discontinuous) changes

in seasonal patterns such as may arise from legal or other types of institutional change.

In a second kind of test the irregular, cyclical, and seasonal components computed from different real economic series by the electronic computer program were combined into artificial series, and the method was applied to these artificial aggregates. That is, the seasonal factor from one series, the cyclical-trend from a second series, and the irregular factor from a third series were combined multiplicatively into an artificial composite. Each of the actual components that had been combined to make up the artificial aggregate (the input) was then compared with the corresponding component yielded by the electronic com-

puter decomposition (the output). Some of the results are shown in Table 1 and Fig. 3.

The artificial series were constructed in such a way as to test the method of extracting each factor (irregular, cyclical, and seasonal) under both favorable and unfavorable conditions. This was accomplished by making up an artificial series in which one factor showed small movements relative to the other two, and another in which the same component had large movements relative to the other two. Altogether ten different artificial series were constructed; for five of these the test was made with the use of both constant and changing seasonal factors.

In most instances the "estimated" com-

ponents trace a course similar to that of the "true" components. Moreover the monthly amplitudes of the "estimated" components usually closely approximate those of the "true" components. Clearly, the electronic computer program has considerable power to rediscover the different types of fluctuations that were built into the series and does not generate arbitrary fluctuations that have no relationship to the original observations.

While the results appear to be generally good, some limitations are also clear: (i) The magnitude of the largest of the three components is almost always reduced, with offsetting increases in one or both of the other factors. (ii) Where one or both of the factors are large rela-

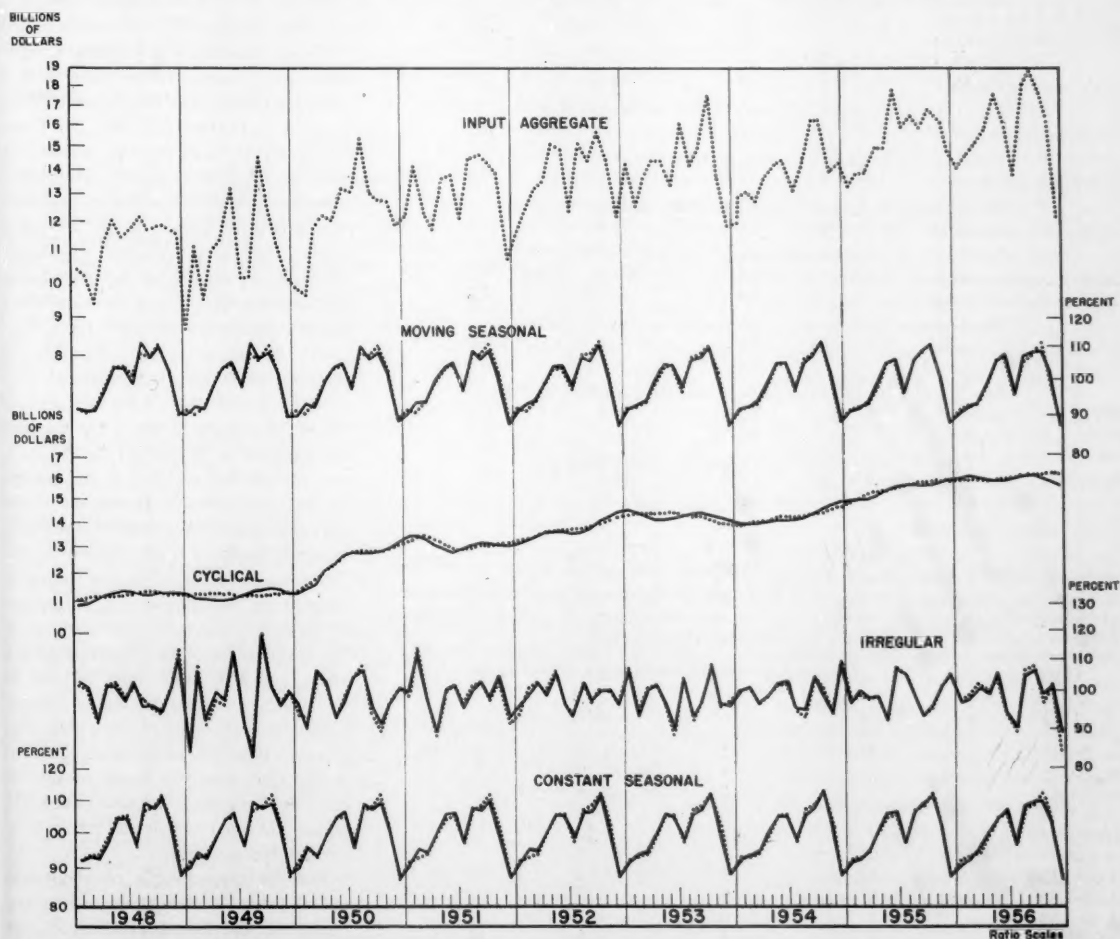


Fig. 3. A number of artificial series were constructed by combining components from various sources as a test of the quality of the Census Bureau method of decomposing economic time series. The series shown above as the input aggregate was made up of (i) an irregular component from the residential building contracts series, Y (ii) a cyclical component from the retail sales series, Z, and (iii) a seasonal component from the freight car loadings series, W. These components are shown as input series (dotted lines). The input aggregate was then decomposed by the computer. The resulting components are shown as solid lines (output). The moving seasonal lines compare a moving seasonal input with a moving seasonal output. The constant seasonal lines compare a constant seasonal input with a moving seasonal output. The same test was applied to nine other artificial series with the results summarized in Table 1.

tive to the third, the smallest factor can be significantly affected. (iii) The amplitudes of the cyclical and seasonal factors tend to be overestimated more (or underestimated less) when relatively large irregular factors are present. The analy-

sis indicates, however, that these deficiencies are important only in kinds of series that occur infrequently at the national level (see Tables 2 and 3). They may be more serious for individual firm data, however. The results also strongly

suggest that the program could be improved by using more powerful smoothing formulae for series with large irregular components. The procedure for choosing among such formulae could be written into the program and thus be made completely automatic. Further tests are planned. In one, the component series would be combined additively, or partly additively and partly multiplicatively. In another, series built up from mathematical components would be decomposed, and the results would be studied.

Table 1. Comparisons of the average monthly amplitudes of the components of artificial aggregates (input) with those yielded by the decomposition of these aggregates (output). In column 1, the first letter indicates the series supplying the irregular factor; the second, that supplying the cyclical factor; the third, that supplying the seasonal factor: *W*, freight-car loadings; *X*, business failures; *Y*, residential building contracts; *Z*, retail sales. The symbols  $\bar{I}$ ,  $\bar{C}$ , and  $\bar{S}$  represent average month-to-month change, without regard to sign, in irregular component, cyclical component, and seasonal component, respectively.

Time series components	Input				Output			
	$\bar{I}$	$\bar{C}$	$\bar{S}$	$\bar{I}/\bar{C}$	$\bar{I}'$	$\bar{C}'$	$\bar{S}'$	$\bar{I}'/\bar{C}'$
<i>Test 1: Moderate irregular and cyclical, large seasonal, factors</i>								
ZZY, moving seasonal	1.7	0.6	11.3	2.8	1.5	0.6	10.6	2.5
ZZY, constant seasonal			9.6				9.6	
<i>Test 2: Moderate irregular and seasonal, large cyclical, factors</i>								
ZXW, moving seasonal	1.7	3.2	5.0	0.5	2.2	2.6	5.1	0.8
ZXW, constant seasonal			5.4				5.5	
<i>Test 3: Moderate irregular, large cyclical and seasonal, factors</i>								
ZXY, moving seasonal	1.7	3.2	11.3	0.5	3.1	2.7	10.3	1.1
<i>Test 4: Large irregular, moderate cyclical and seasonal, factors</i>								
YZW, moving seasonal	7.8	0.6	5.0	13.0	7.6	0.8	5.3	9.5
<i>Test 5: Large irregular and cyclical, moderate seasonal, factors</i>								
YYW, moving seasonal	7.8	2.7	5.0	2.9	7.4	2.6	5.5	2.8
<i>Test 6: Large irregular, moderate cyclical and seasonal, factors</i>								
XZW, moving seasonal	15.3	0.6	5.0	25.5	14.8	1.3	5.9	11.4
<i>Test 7: Large irregular and seasonal, moderate cyclical, factors</i>								
XZY, moving seasonal	15.3	0.6	11.3	25.5	14.8	1.3	10.7	11.4
XZY, constant seasonal			9.6				9.9	
<i>Test 8: Large irregular and cyclical, moderate seasonal, factors</i>								
XXW, moving seasonal	15.3	3.2	5.0	4.8	14.8	3.2	5.8	4.6
XXW, constant seasonal			5.4				6.0	
<i>Test 9: Large irregular and cyclical, moderate seasonal, factors</i>								
XYZ, moving seasonal	15.3	2.7	6.5	5.7	14.7	2.6	7.0	5.7
XYZ, constant seasonal			6.8				6.8	
<i>Test 10: Large irregular, cyclical, and seasonal, factors</i>								
XXY, moving seasonal	15.3	3.2	11.3	4.8	13.8	3.1	11.1	4.5

Table 2. Relative magnitude of seasonal, irregular, and cyclical factors in 149 economic series, 1947-1956. The symbols  $\bar{S}$ ,  $\bar{C}$ ,  $\bar{I}$ , and  $\bar{C}/\bar{I}$  represent average month-to-month percentage change, without regard to sign, in seasonal component, cyclical component, irregular component, and seasonally adjusted data, respectively.

Class interval (%)	Percentage distribution of series, according to			
	$\bar{S}/\bar{C}/\bar{I}$	$\bar{S}/\bar{I}$	$\bar{S}/\bar{C}$	$\bar{I}/\bar{C}$
0-0.19	1	1	0	0
0.20-0.39	1	1	0	3
0.40-0.59	15	4	5	5
0.60-0.79	21	10	5	10
0.80-0.99	17	18	12	7
1.00	0	1	0	1
1.01-1.19	9	17	5	10
1.20-1.39	8	9	5	5
1.40-1.59	3	6	1	2
1.60-1.79	3	4	4	5
1.80-1.99	2	3	3	5
2.00-2.99	9	10	15	18
3.00-3.99	4	5	11	14
4.00-4.99	5	6	11	7
5.00 and over	2	5	23	8
Totals	100	100	100	100

## Findings: Relations among Types of Economic Fluctuations

A sample of about 150 series, selected as broadly representative of the different activities of the United States economy, has been decomposed and studied. The cyclical, seasonal, and irregular amplitudes are summarized in Table 2 and shown in detail for 18 important monthly business indicators in Table 3. These tables reveal that, for the post-World War II period, seasonal movements dominate other kinds of month-to-month movements in most current economic series. Seasonal movements are almost always larger than either the irregular or cyclical movements, and they are often larger than both of the other types combined. More specifically, the average monthly amplitude of the seasonal fluctuations exceeds that of the cyclical factor in 78 percent of the series, exceeds the irregular in 65 percent of the series, and exceeds the cycle-trend and irregular in combination in 45 percent of the series. Furthermore, where the seasonal factor is larger, it is often much larger. The seasonal factor is 3 or more times as large as the cyclical factor in 45 percent of the series, 3 or more times as large as the irregular factor in 16 percent of the series, and 3 or more times as large as the cyclical and irregular fluctuations together in 11 percent of the series. The relative magnitude of the seasonal factor is also very great in many of the 18 monthly business indicators (Table 3) which are used widely in interpreting current business trends.

For the same sample of about 150 series, ratios of the average irregular change to the average cyclical change were computed for 1-, 2-, 3-, 4-, 5-, and 6-month spans. Separate computations were made for the interwar period, 1919-1939, and the postwar period, 1947-1956. The distribution of the measure showing the months required for cy-



dical dominance (MCD), given in Table 4, provides a broad view of the relations between the irregular and the cyclical factors in U.S. economic series. This table shows that on a month-to-month basis, the average change in the irregular factor is larger than that in the cyclical factor in about 75 percent of the series; over 3-month intervals it is larger in about 25 percent of the series; over 6-month intervals it is larger in less than 10 percent of the series.

These results emphasize the advantages of seasonally adjusted series for studying cyclical movements over those not so adjusted. Where the seasonal fluctuations are large, a difference in the unadjusted data for two months may be due largely or solely to normal seasonal fluctuations; if the data are seasonally adjusted, the difference can be assumed to be caused chiefly by cyclical or irregular factors. The results also emphasize the importance of knowledge of the relative magnitudes of irregular and cyclical factors in interpreting current move-

ments in economic series. They indicate that the month-to-month movements of most seasonally adjusted series are not "cyclically significant"; for most series, meaningful economic trends are revealed only by comparisons over three-month or longer spans. For many series, of course, month-to-month changes are significant, and this group includes such important series as total industrial production and total nonagricultural employment. The measure MCD provides a useful guide for interpreting the short-term fluctuations of each series.

It should be noted that more frequent observations make more current comparisons possible. Consider a series in which the cyclical factor does not dominate until comparisons are made over 3-month periods. If this series is available quarterly, only one comparison a quarter can be made. If it is available monthly, then three comparisons a quarter can be made: the first month of each quarter with the first month of the preceding quarter, the second month of

Table 4. Months required for cyclical factor to dominate the irregular factor in 150 important economic series, 1919-1939 and 1947-1956.

Months required for cyclical factor dominance	Percentage distribution of 150 series according to measure, MCD	
	1919-1939	1947-1956
1	23	27
2	29	21
3	25	23
4	14	11
5	5	10
6 or more	4	8
Total	100	100

each quarter with the second month of the preceding quarter, and the third month of each quarter with the third month of the preceding quarter. Thus, seasonally adjusted weekly series may add to the currency of economic information, even though the week-to-week fluctuations are not significant.

Other important findings can be discerned from these tables and from the listing (not given here) of the measures for each series in the sample. There is a high correlation between the magnitude of the amplitudes of the irregular, seasonal, and cyclical factors: Series with large irregular movements generally also have large cyclical and large seasonal movements. This implies some systematic relationship among the month-to-month forces represented by the irregular series, the annual forces represented by the seasonal series, and the longer-term forces represented by the cyclical-trend series. Furthermore, series which usually lead at business-cycle turning points usually have large irregular, seasonal, and cyclical fluctuations; series that are usually coincident at cyclical turning points usually have moderate fluctuations; and series that usually lag at turning points usually have small fluctuations (see especially Table 3). That is, series which respond promptly to prospective changes in business conditions also respond vigorously, and series which respond sluggishly also respond mildly.

These findings raise interesting new questions about the relations among the causes of economic fluctuations.

#### References and Notes

1. This article is an adaptation of more detailed statements appearing in economic and statistics journals, as follows: (i) J. Shiskin, "Electronic computers and business indicators," *J. Business* (Oct. 1957), republished as *Occasional Paper No. 57* by the National Bureau of Economic Research, New York, N.Y.; (ii) J. Shiskin and H.

Table 3. Relative magnitude of the seasonal, irregular, and cyclical factors in 18 monthly business indicators, 1947-1956. The symbols  $\bar{S}$ ,  $\bar{I}$ ,  $\bar{C}$ , and  $\bar{CI}$  represent average month-to-month percentage change, without regard to sign, in seasonal component, irregular component, cycle-trend component, and seasonally adjusted data, respectively. The "leading series" usually anticipate changes in general business conditions; the "coincident series" usually delineate changes in general business conditions; the "lagging series" usually follow changes in general business conditions [see G. H. Moore, "Statistical indicators of cyclical revivals and recessions," *Natl. Bur. Econ. Research Occasional Paper No. 31* (1950)].

Series	$\bar{CI}$	$\bar{I}$	$\bar{C}$	$\bar{S}$	$\bar{S}/\bar{CI}$	$\bar{S}/\bar{I}$	$\bar{S}/\bar{C}$	$\bar{I}/\bar{C}$
<i>Leading series</i>								
1. Business failures, liabilities	16.6	15.7	3.2	10.0	0.6	0.6	3.1	4.9
2. Industrial stock prices	2.0	1.5	1.2	1.0	0.5	0.7	0.9	1.2
3. New orders, durable manufactures	5.3	4.8	2.0	6.2	1.2	1.3	3.0	2.3
4. Residential building contracts	8.6	8.0	2.8	11.2	1.3	1.4	4.0	2.9
5. Commercial and industrial building contracts	13.5	12.8	3.0	10.6	0.8	0.8	3.6	4.3
6. Hours worked, manufacturing	0.4	0.3	0.2	0.5	1.4	1.8	2.8	1.6
7. New incorporations	4.3	4.0	1.3	8.4	2.0	2.1	6.7	3.2
8. Wholesale prices, basic commodities	2.2	1.4	1.3	1.2	0.6	0.9	1.0	1.1
<i>Coincident series</i>								
9. Nonagricultural employment	0.4	0.2	0.3	0.8	2.0	3.8	2.6	0.7
10. Unemployment, total	5.4	4.0	3.0	9.4	1.7	2.4	3.2	1.3
11. Bank debits outside New York City	3.1	3.0	0.8	6.1	2.0	2.0	7.7	3.8
12. Freight carloadings	3.4	3.0	1.2	5.1	1.5	1.7	4.4	2.6
13. Industrial production	1.1	0.7	0.8	2.3	2.1	3.4	3.0	0.9
14. Nonfarm wholesale prices, exclusive of foods	0.4	0.2	0.4	0.2	0.5	1.3	0.6	0.4
<i>Lagging series</i>								
15. Personal income	0.8	0.6	0.6	4.5	5.5	8.1	7.8	1.0
16. Retail sales	1.9	1.7	0.6	6.5	3.4	3.8	11.6	3.1
17. Instalment credit outstanding	1.7	0.3	1.7	0.8	0.4	2.3	0.4	0.2
18. Inventories of manufacturers	0.9	0.2	0.9	0.4	0.4	1.5	0.4	0.3

Eisenpress, "Seasonal adjustments by electronic computer methods," *J. Am. Statist. Assoc.* (Dec. 1957), reprinted as *Technical Paper No. 12* by the National Bureau of Economic Research, New York, N.Y.; and (iii) J. Shiskin, "Seasonal adjustments of economic indicators," *Proc. Business and Econ. Sect. Am. Statist. Assoc.* (1957). The project described in this article has been carried on at the Bureau of the Census since the spring of 1954. During the academic year 1956-57, however, I extended and refined the electronic computer program during a year's leave of absence spent at the

National Bureau of Economic Research. The tests of the program and the analysis of the relations among different types of economic fluctuations described were both made during this academic year. This work was financed by National Science Foundation and Rockefeller grants. Important contributions to this project have been made by Henry Eisenpress and Geoffrey H. Moore. Michael J. Conlon provided valuable assistance in the preparation of this article.

2. J. Shiskin, "New measures of recession and recovery," in preparation.

3. The method of time series decomposition described here follows the general plan formulated by early analysts of economic time series, particularly Warren M. Persons [see W. M. Persons, "Indices of business conditions," *Rev. Econ. and Statistics* (Jan. 1919); "An index of general business conditions," *ibid.* (Apr. 1919)].
4. For other tests, see the sources cited in (1).
5. The results for six additional series are shown in J. Shiskin and H. Eisenpress, "Seasonal adjustments by electronic computer methods," *J. Am. Statist. Assoc.* (Dec. 1957), pp. 432-433, chart 6.

## Radiation Dose Rate and Mutation Frequency

The frequency of radiation-induced mutations is not, as the classical view holds, independent of dose rate.

W. L. Russell, Liane Brauch Russell, Elizabeth M. Kelly

It is usually considered to be one of the basic tenets of radiation genetics that variation in radiation intensity—that is, dose rate—does not affect mutation rate. However, the experimental results upon which this conclusion is based were obtained only from certain cell stages, particularly *Drosophila* spermatozoa. The bulk of the radiation dose causing genetic hazards in man will be accumulated not in spermatozoa but in spermatogonia and oocytes. It was therefore of both practical and fundamental importance to question whether mutation rates observed following irradiation of these cell stages would also prove to be independent of radiation intensity.

Two major considerations that prompted such a question, in the face of the general acceptance of the absence of a radiation intensity effect on induced mutation rate, may be outlined. First, there has been increasing evidence that induction of mutation may not be as direct an action as had often been supposed, and that the mutation process in the gene may not be entirely independent of variation in its cellular environment. Consequently,

there was room for speculation that even though the mutation process in spermatozoa is apparently independent of dose rate, it might not be so in metabolically active cells like spermatogonia. Second, it was reasoned that even if the actual mutation process in spermatogonia should prove to be, as in spermatozoa, independent of radiation intensity, nevertheless the mutation rate, as measured by mutations transmitted to the offspring, might still be dependent on dose rate, because of cell selection due to killing or other interference with the dynamics of the cycle of the seminiferous epithelium (1, 2).

With these two considerations in mind, experiments to determine mutation rates induced by chronic gamma irradiation in spermatogonia in mice were started. The first data from these experiments, and a comparison of them with mutation rates obtained earlier with acute x-irradiation, were presented at the April 1958 annual meeting of the National Academy of Sciences (1). They had been submitted earlier for a publication still in press (2), and they have also been discussed briefly elsewhere (3). The results showed a much lower mutation rate from chronic gamma than from acute x-irradiation. It

was pointed out that, without further analysis, it could not be definitely decided whether the difference was attributable to intensity or to quality of radiation (although the latter seemed unlikely in view of the magnitude of the effect), and whether it was the mutation process itself that was involved or some secondary process, such as cell selection.

Since the time of the early reports, the data have been approximately doubled. Also, a number of new experiments, undertaken specifically for the purpose of analyzing the observed effect, have already thrown additional light on the problem. Because of the wide interest in this field, the present interim report has been prepared, bringing tabulation of the spermatogonia results up to date and presenting preliminary results from the new experiments.

### Chronic Gamma Irradiation of Spermatogonia

Young mature male mice were exposed, in polystyrene cages of 3.0 to 3.5-millimeter wall thickness (more than adequate for secondary electron equilibrium), to a 5-curie Cs<sup>137</sup> source. Dose rate was regulated by distance. Exposure was continuous (except for occasional interruptions of a few minutes) until the total dose had been accumulated (4). The males were mated to test females (see below) immediately following removal from the radiation field. However, only mutations induced in spermatogonia are considered in this section of this article. Unirradiated males were tested simultaneously with the irradiated.

Mutation rates were determined by the specific locus method. Irradiated and control males are mated to females homozygous for seven autosomal recessive visibles. The offspring are then examined for mutations at the seven loci. Details of the experimental procedure have been described earlier (5).

The results from the chronic gamma irradiation experiments are given in

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Table 1. The mutations listed in the table have not yet all been tested for allelism. However, classification by phenotype has proved remarkably reliable in our experience with well over 100 tested mutants at these loci, so there is little likelihood of error.

For comparison with the chronic gamma irradiation data listed in Table 1, a summary is presented in Table 2 of the results of three of our acute x-ray experiments (2). The radiation intensity in these experiments was approximately 80 to 90 roentgens per minute.

Results from the chronic gamma and acute x-ray experiments are compared in Fig. 1. All the points for the chronic gamma-ray mutation rate curve are considerably below the acute x-ray curve. However, a comparison of the two sets of results over the whole range of doses cannot be reduced to a simple statistical test of significance because the mutation rate curve following acute x-irradiation shows a clear departure from linearity, already discussed elsewhere (2, 3, 6), while the present mutation rate data from chronic gamma irradiation show no evidence of a similar departure. Three statistical tests have been made (7) which attempt to avoid this difficulty in different ways.

In view of the possible special reasons for the departure of the acute x-ray curve from linearity (the drop in the mutation rate at the 1000-roentgen dose being attributed to cell selection), one test of the significance of the difference between the chronic gamma and acute x-radiation induced mutation rates was made with the 1000-roentgen x-ray point excluded. The two sets of data, with a combined control point, were fitted simultaneously to two straight lines by the method of least squares, with weights based on the Poisson assumption. The ratio of the slopes is 4.1 (95-percent confidence interval 2.36, 12.5), and the slopes differ significantly ( $P < 1 \times 10^{-9}$ ). A similar test, but one that excludes both the acute x-ray 1000-roentgen point and the chronic gamma-ray 861-roentgen point, also yields a significant difference ( $P < 1 \times 10^{-7}$ ). The third statistical test was made between just two points. In view of the lack of data at closely comparable doses in the lower part of the dose range, and because of the presumed complexity at the 1000-roentgen x-ray point, the two points that seemed to offer the most meaningful single comparison were the 600-roentgen point for acute x-rays and the 516-roentgen point for chronic gamma

Table 1. Mutations at specific loci induced in spermatogonia of mice by chronic gamma irradiation.

Dose (r)	Intensity (r/wk)	Off-spring (No.)	Mutations at 7 loci (No.)	Mean No. of mutations per locus, per gamete ( $\times 10^5$ )
0		105,403	8	1.08
86	10	48,500	6	1.77
516	90	20,752	4	2.75
861	90	20,993	9	6.12

Table 2. Mutations at specific loci induced in spermatogonia of mice by acute x-irradiation.

Dose (r)	Off-spring (No.)	Mutations at 7 loci (No.)	Mean No. of mutations per locus, per gamete ( $\times 10^5$ )
0	42,833	1	0.33
300	40,408	25	8.85
0	106,408	6	0.81
600	119,326	111	13.29
0	33,972	2	0.84
1000	31,815	23	10.33

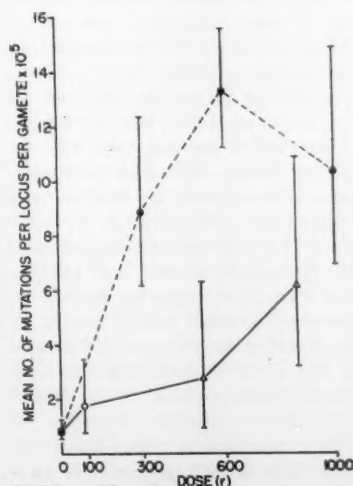


Fig. 1. Mutation rates at seven specific loci in the mouse, with 90-percent confidence intervals. Solid circles represent results with acute x-rays (80 to 90 r/min). Open points represent chronic gamma-ray results (triangles, 90 r/wk); (circle, 10 r/wk). The point for zero dose represents the sum of all controls.

rays. A test of the significance of the difference between the mutation rates per roentgen at these two points gave  $P = 0.0008$  for a one-tailed test (8).

In the statistical tests, the fitted curves show no evidence of departure from linearity. The question of whether or not the data may be expected to be truly linear is discussed below. The actual ratio of effectiveness of chronic gamma and acute x-irradiation found may, of course, be valid only for the particular combination of doses and intensities tested. The important point is that the data now available adequately confirm the earlier report (1-3) that chronic gamma radiation is significantly less effective than acute x-radiation in inducing specific locus mutations in spermatogonia.

The conclusions of the preceding paragraphs—that chronic gamma irradiation of mouse spermatogonia is mutagenically less effective than acute x-irradiation—is in sharp contrast to the findings for *Drosophila* spermatozoa, reviewed by Muller (9), which have heretofore been considered to have general applicability and have entered into the basic concepts of radiation genetics.

It is, therefore, of great importance to attempt to determine what factors are responsible for the present result. For this reason, a number of experiments, designed to throw light on this question, have been initiated. In Table 3, preliminary results of these new experiments, as well as older findings already reported elsewhere, are compared with the present data.

### Intensity versus Quality

The difference in mutation rate between spermatogonia subjected to chronic gamma irradiation and those subjected to acute x-irradiation could be due to differences either in quality or in intensity of radiation. In order to differentiate between these two factors, the effect of a change in quality alone has been investigated in three separate comparisons (see Table 3). No appreciable differences were found in the effectiveness of acute gamma rays (from  $\text{Co}^{60}$ ), on the one hand, and acute x-rays, on the other, in inducing dominant lethal mutations in spermatozoa, specific locus mutations in spermatozoa and other post-spermatogonial stages, or specific locus mutations in spermatogonia. (It appears safe to assume the same result also for oocytes, for which no direct quality com-

Table 3. Semiquantitative comparison of mutation rates presented in this article with those obtained earlier and with preliminary results from experiments in progress. Each plus symbol in the table stands for a mutation rate of approximately  $5 \times 10^{-8}$  per roentgen, per locus. The check marks represent arbitrary values that are valid for comparative purposes among the dominant lethal results. They cannot be quantitatively compared with the specific locus mutation rates.

Gametogenic stage irradiated	Genetic effect measured	Type of irradiation		
		Chronic Gamma (Cs <sup>137</sup> )	Acute	
			Gamma (Co <sup>60</sup> )	X-ray
Postspermatogonia	Dominant lethals*†	✓ ✓ ✓	✓ ✓ ✓	✓ ✓ ✓
Postspermatogonia	Specific locus mutations	(+++++)‡	+++++++§	+++++++
Spermatogonia	Specific locus mutations	+	++++§	+++
Oocytes	Specific locus mutations	+		+++++**

\* Paper in preparation.

† Chronic and acute gamma rays give approximately equal rates, although comparison is not exact because of difficulty in matching particular postspermatogonial stages irradiated. In the comparison of acute gamma with acute x-rays, the former were found slightly less effective.

‡ Value is based on only 1 mutation in 1613 young, so the mutation rate is not yet reliable.

§ Value based on 4 mutations.

|| From Russell *et al.* (17).

¶ From Russell *et al.* (12); see also Carter (13) for chronic Co<sup>60</sup> gamma data.

\*\* From Russell *et al.* (18).

parison was made.) These results show that difference in the quality (linear energy transfer) of the gamma rays and x-rays tested, while it may account for a small part, cannot account for the bulk of the difference between the chronic gamma and acute x-ray mutation rate results. It can be concluded that most of the difference must be due to intensity of radiation.

#### Intensity and Gametogenic Stage

The results summarized in Table 3 show that radiation intensity effects were found only for spermatogonia and oocytes. In the experiments with postspermatogonial stages, radiation intensity had no appreciable effect on the yield of genetic changes. This conclusion can be drawn with near certainty for dominant lethals. The specific locus data, from experiments still in progress, are not yet extensive, but, as far as they go, they are not in disagreement with the dominant lethal result. In both cases, the stages irradiated were spermatozoa and spermatids, with the bulk of the data from the former. It may thus be concluded that dose rate does not influence the frequency of genetic changes produced by irradiation in mouse spermatozoa, but conclusions regarding spermatids and spermatocytes will have to await further work. The spermatozoa results are in agreement with the findings for *Drosophila* spermatozoa. Thus, the classic

finding of intensity independence is supported for spermatozoa (10). The explanation for the new phenomenon of intensity dependence resides in gametogenic stage.

#### Mutation Process versus Cell Selection

The intensity effect in spermatogonia might have been due to secondary causes—that is, selection as a result of cell killing or other interference with the dynamics of the cycle of the seminiferous epithelium, as stated above. This was put forward as one plausible, but not favored, hypothesis in the first detailed publication of the data (2). This hypothesis has now been deliberately tested by new experiments on females. Since oogenesis are not present in the adult ovary (11), and since the completion of the first meiotic division only just precedes ovulation, radiation genetic experiments on adult females deal exclusively with primary oocytes, and the bulk of these are in the uniform dictyate state. Results already reported (2, 12) showed that chronic gamma irradiation of oocytes gave mutation rates lower than those from acute x-irradiation of spermatogonia. The new results (Table 3) indicate that acute irradiation of oocytes is at least as effective as acute irradiation of spermatogonia.

In the light of this finding of a dose-rate effect for oocytes as well as for spermatogonia, the hypothesis that the in-

tensity effect on mutation rate is due to cell selection appears to be less tenable. Since oocytes are nonmitotic, since the stages irradiated show no obvious variability, and since, in our chronic irradiation experiment, the continued fertility of the females provides no evidence of extensive killing, selective or otherwise, of the oocytes, it seems highly unlikely that the difference between the mutation rates following chronic and acute irradiation of oocytes can be attributed to any secondary mechanism similar to that put forward as a possible one for spermatogonia. Of course, this mechanism might still be postulated as playing a role in the spermatogonia results, but it is simpler to assume that the explanation for the results in oocytes—namely, that the intensity effect is on the mutation process itself—also applies to spermatogonia.

It should be noted that, at each dose rate tested, there is at present no evidence of marked difference between oocytes and spermatogonia in sensitivity to mutation induction. Therefore, the interpretation by Carter (13), who also found a low mutation rate with chronic gamma irradiation of oocytes, and who thought it most likely that this was attributable to sex, is not upheld. His emphasis on the consequence of his interpretation—namely, that only a small part of the genetic hazard from medical irradiation would come from exposure of females—must now be discounted.

#### Relation to the Linearity Concept

The various results discussed in the three preceding sections and summarized in Table 3 have determined which among the possible factors are the ones responsible for the lower mutation rate from chronic gamma irradiation. It turns out that these are also the more interesting factors. Two of these are radiation intensity, rather than quality; and the mutation process itself, rather than cell selection. Since the finding of an intensity effect on the mutation process was unexpected, the field is now open for new hypotheses about the nature of this process. Such hypotheses are aided, or at least delimited, by the finding of a third factor—namely, that the intensity effect occurs in spermatogonia and oocytes, but apparently not in spermatozoa. Thus, the mechanism for this effect may be found among the characteristics by which the highly specialized spermatozoa differ from spermatogonia and oocytes.



Speculation concerning the nature of the mutation process has a direct bearing on the fundamental problem of what the mutation rates are now likely to be at other doses and intensities. One specific question is already being debated—namely, whether or not the finding of an intensity effect in spermatogonia and oocytes is strong indication that a threshold dose will be found for mutation induction in these cells. This possibility has obvious and vital importance to the problem of genetic hazards.

A strong argument that has long been advanced against the threshold concept is the likelihood that a single direct hit (ion or ion cluster) on such a small target as a gene must sometimes be adequate to cause mutation. This hypothesis has not only seemed plausible on physical grounds but has also been supported by the mutation rate data for *Drosophila* spermatogonia and for other material where an intensity independence or a linear relation with dose has been found (9). The new data from mouse spermatogonia provide additional support. If the intensity effect reported here for mouse spermatogonia and oocytes is taken as evidence for a threshold effect for all mutations induced in these cells, then this necessarily implies that all mutations in spermatogonia and oocytes are induced by a process different from that which has long been, and still can be, assumed for spermatogonia. This may be true, but it would certainly be incautious to jump to this conclusion. In fact, it seems quite plausible to assume that spermatogonia and oocytes may not be completely different from spermatogonia—in other words, that at least a portion of the mutations in them may be induced by a single-hit process.

To make the consequences of this hypothesis easily understandable, they will be presented in terms of a specific model. Thus, it can be postulated that there are two kinds of mutation which, for simplicity in the following discussion, will be called "reparable" and "irreparable." (They could, alternatively, and perhaps more realistically, be looked upon as "preventable" and "not preventable.") It can be further assumed that in spermatogonia and oocytes there is repair of the reparable mutations at the low radiation-intensity (chronic) level so far tested. Such repair is assumed to be impossible, or less probable, because of radiation damage to the repair process, at high radiation intensities (acute) in spermatogonia and oocytes. Repair is also assumed to be impossible at all in-

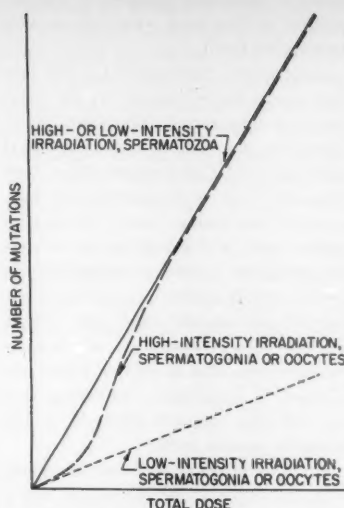


Fig. 2. Theoretical dose curves constructed on the basis of the hypothesis (see text) that "repair" of some mutations is possible in spermatogonia and oocytes but not in spermatogonia.

tensities in spermatogonia, perhaps because of some property—for example, a metabolic activity—lacking in them that is present in spermatogonia and oocytes.

Such a hypothesis could lead to a set of curves something like that shown in Fig. 2. The straight line for chronic irradiation of spermatogonia and oocytes is assumed to be the single-hit curve for irreparable mutation, all reparable ones having been repaired. A steeper straight line is shown for spermatogonia, where it is assumed that none of the reparable mutations are repaired and that both these and the irreparable ones follow a single-hit relation with dose, regardless of intensity. It follows logically that, as is shown in the third curve, acute irradiation of spermatogonia and oocytes would, at total doses low enough to permit repair, duplicate the curve for chronic irradiation, but that, at higher doses, when repair fails, the curve would shift over to a new position approaching that for spermatogonia. (Actually, the curve for observed mutations in spermatogonia is much steeper than the curve for acute irradiation of spermatogonia. The reasons for this, one of which is probably a large chromosomal aberration component of the mutations in spermatogonia (14), are assumed to be irrelevant to the present argument. In Fig. 2, the curve for spermatogonia, as well as the curve for oocytes, may be looked upon as being appropri-

ately adjusted to eliminate the irrelevant factors and to provide an uncomplicated comparison for radiation intensity only.)

No importance is attached to the particular details chosen to make this type of model easily understandable. Thus, "reparable" and "irreparable" need not imply qualitatively different mutational sites. Only one kind of site is necessary if, for example, it is assumed that there is a time lag for the completion of the mutation process and (even with the repair process intact) a probability of less than unity that repair could occur before this completion. Also, the term *repair* is not necessarily restricted to mean the reversal of a damaged gene to normal. In fact, as was mentioned earlier, the term *preventable* might be substituted in place of *reparable*. Prevention could occur at any stage in the mutation process, even at its initiation when there might be diversion, by a "lightning-rod" effect, of ions that might otherwise have caused mutation.

Whether or not the proposed hypothesis is favored, it demonstrates clearly that the discovery of an intensity effect does not necessarily imply that all induced mutations in spermatogonia and oocytes must follow a threshold response. Of course the hypothesis does involve a threshold concept, but it applies to only a portion of the mutations. As demonstrated, the theoretical consequence for chronic irradiation of spermatogonia and oocytes, in this particular model, is a linear relation between mutation rate and dose, even down to the lowest doses, in spite of a lower mutation rate than with acute irradiation.

Other plausible models can, of course, be constructed. Experiments now under way with various intensities of radiation and with fractionated doses will undoubtedly narrow down the possibilities. It should be noted, however, that the range of intensities already tested is tremendous—namely, 10,000-fold (100,000-fold at one point). The fact that this has yielded only a fourfold difference in mutation rate certainly raises the question of whether a further decrease in intensity would be likely to give a further drop in mutation rate. The mutation rate at the lowest intensity tested—10 roentgens per week—and the rate reported by Carter *et al.* (15) for a similar intensity still have such wide confidence intervals that they are not particularly informative in a comparison with the results from the 90-roentgen-per-week intensity.

## Human Hazards

Caution must be exercised against reaching dangerous conclusions from the present results. Thus, as has been emphasized, it is not safe to conclude that the data imply a threshold dose for all mutations in spermatogonia and oocytes. There might not even be any further reduction in mutation rate with further decrease in intensity. Furthermore, it should not be forgotten that even the lower mutation rates obtained with the present intensity levels are still appreciable and at least as high as *Drosophila* rates for acute irradiation. However, from the results as they stand—results that apply to the germ-cell stages (spermatogonia and oocytes) that are important in appraising human hazards—it does seem safe to conclude that, with at least some intensities of radiation, the genetic damage would not be as great as that estimated from the mutation rates obtained with acute irradiation.

## Summary

New data have clearly confirmed the earlier finding that specific locus mutation rates obtained with chronic gamma irradiation of spermatogonia are lower than those obtained with acute x-rays. Since this result is in contrast to classical findings for *Drosophila* spermatozoa, and apparently contradicts one of the basic

tenets of radiation genetics, it was important to determine what factors were responsible for it.

Experiments undertaken for this purpose reveal the following: (i) the lower mutation frequency is due mainly to difference in dose rate of radiation, rather than quality; (ii) a dose-rate effect is not obtained in experiments with mouse spermatozoa, confirming classical findings for spermatozoa, and indicating that the explanation for intensity dependence in spermatogonia resides in some characteristic of gametogenic stage; and (iii) a dose-rate effect is found not only in spermatogonia but also in oocytes, where cell selection is improbable, indicating that the radiation intensity effect is on the mutation process itself.

A threshold response for all mutations in spermatogonia and oocytes is not a necessary consequence of the findings. Plausible hypotheses consistent with the present results can lead to other predictions.

From a practical point of view, the results indicate that the genetic hazards, at least under some radiation conditions, may not be as great as those estimated from the mutation rates obtained with acute irradiation. However, it should not be forgotten that even the lower mutation rates obtained with the present intensity levels are still appreciable (16).

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# Groningen Radiocarbon Dates III

H. de Vries and H. T. Waterbolk

The present series of radiocarbon dates obtained at the University of Groningen covers the period from March 1956 to August 1957. The first two lists (I, 2) will be referred to as I and II. Characteristics of the counters and descriptions of the technical procedures, statement of errors, and so forth, were given in list II.

Samples numbered between 600 and 900 were measured in the small counter; samples numbered between 500 and 600

and between 1200 and 1500 were measured in the large counter; and samples between 900 and 1200 and above 1500 were measured in the medium-sized counter.

Measurements on the radioactivity of shells and snails from different environments during the last 4 years have been published separately (3), since they are not given "dates." One of the conclusions drawn from these measurements is that

the amount of carbon-14 in the atmosphere increased by about 5 percent between the end of 1953 and the spring of 1957. This increase is due to the explosions of atomic bombs. A group of Würm interstadial samples has been published separately (4), since they require a more detailed discussion. The results can be summarized briefly as follows: About 26,000 years ago a fairly short interstadial (or warmer oscillation) occurred, which produced the Paudorf fossil soil. The first Würm interstadial occurred at about 50,000 years ago, no indication of a warmer period between 50,000 and 26,000 years ago being found up to now.

The remaining dates are given here in four groups (Tables 1-4). The first group consists of a series of geological samples from northwestern Europe; it

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includes some standard sections and datings of pollen zones. Group 2 deals with archeological samples from Europe. Group 3 deals with archeological samples outside of Europe; and group 4 deals with special problems.

Since completion of the present list, a careful study has been made of a series of samples of known age (5). It was

found that the activity of radiocarbon in the atmosphere was going up and down even before the Industrial Revolution. This affects the dating results in a complicated way which cannot yet be taken into account here. Our recent standard turned out to be about 3 percent too low in activity relative to the average of the samples from between A.D. 1500 and

1800. As a first correction, 240 years should be added to all Groningen radiocarbon dates published up to now, including those in the present list. Besides this general correction, another correction, which may amount to 100 years, has to be applied. This may be in either direction, and it depends in an irregular way on the age of the sample.

Table 1. Geological problems, including the dating of pollen zones (from "standard profiles"). All ages are given in radiocarbon years before the present.

Description	Sample No.	Age	Description	Sample No.	Age
<i>Roggendorf</i> , near Melk (Austria). Peat layer, underlying mud and redeposited löss and supposed to be of interstadial age (6). Submitted by F. Brandtner, Vienna.			Gyttja (-3.70); decrease of quercetum mixtum, increase of <i>Pinus</i> .	Gro-704	6670 ± 145
Upper sample (3.15 to 3.30 m).	Gro-1301	7760 ± 120	Gyttja (-5.10); start of quercetum mixtum.	Gro-703	8160 ± 190
Other part of upper sample.	Gro-1186	8100 ± 100	Gyttja (-7.00); beginning of Allerød.	Gro-688	11,585 ± 200
Lower sample (4.20 to 4.35 m).	Gro-1198	11,400 ± 90	Gyttja (-7.50); middle of Bölling.	Gro-702	12,830 ± 280
Since recent contamination of the samples is nearly impossible, the peat layer is obviously of late- and postglacial age. The pollen diagram does not completely exclude this possibility.			Gyttja (-7.70); beginning of Bölling.	Gro-708	12,660 ± 220
<i>Laacher See</i> (Eifel, Germany). Piece of wood cut out of a charred beam (diameter 20 cm), found in the volcanic Trass in the Brohltal. The trass belongs to the great middle Allerød eruption of the Laacher See.	Gro-1184	11,025 ± 90	Laguna Arroyas (Lago de Sanabria, Zamora, Spain). Gyttja (-5.35); mixture of <i>Pinus</i> , <i>Betula</i> , and quercetum mixtum throughout the section.	Gro-705	13,700 ± 300
Submitted by B. Frechen, Bonn.			<i>Buelna</i> (Asturias, Spain). Peat (-0.50); start of continuous <i>Fagus</i> curve, last decrease of <i>Corylus</i> .	Gro-1078	7360 ± 65
Charred wood found at a depth of about 5 m in the volcanic Trass in the Gleesertal. The flora of this Trass contains some thermophilous species which previously had not been found in the Allerød in Germany. Therefore, a Boreal age of the corresponding eruption was supposed. Collected by J. Schweitzer and submitted by R. Brinkman, Bonn.	Gro-1199	10,680 ± 85	Peat (-0.72); start of <i>Corylus</i> increase.	Gro-1075	2260 ± 45
It is interesting to recall the date of the volcanic eruption in the Schalkenmehrer Maar, already published (2) (Gro-961, age 10,550 ± 100 yr). The Brohltal date falls according to expectation well within the Allerød period. The Gleesertal date, however, corresponds to that of the Schalkenmehrener Maar and belongs to the Younger Dryas time. Apparently, in this period the climate in the area was better than could be concluded from the available botanical evidence. There is thus no proof for postglacial volcanic activity in the Eifel.			<i>Montes del Buayo</i> (Galicia, Spain). Peat (-2.70).	Gro-1076	1775 ± 65
<i>Standard pollen diagrams from Spain</i> . The samples were collected and submitted by J. Menendez Amor (Madrid) and F. Florschütz (Velp, Netherlands), who also prepared the pollen diagrams. Details are being published (7).			<i>Torreblanca</i> (Castellón de la Plana, Levante, Spain). Peat (-0.90).	Gro-1077	7830 ± 75
<i>Laguna de las Sanguijuelas</i> (Lago de Sanabria, Zamora, Spain). Seven samples from a former lake, filled with 8 m of lacustrine and peat deposits. Some of the gyttja samples contained less than 1 g of carbon.			Peat (-2.40).	Gro-1073	1670 ± 45
Peat (depth, -0.50 m); start of strong increase of quercetum mixtum, decline of <i>Pinus</i> .	Gro-687	720 ± 90	Peat (-4.20).	Gro-1074	4120 ± 60
Peat with gyttja (-1.90); <i>Quercus</i> and <i>Pinus</i> dominant.	Gro-709	4270 ± 120		Gro-1072	6280 ± 85
	Gro-1002	4190 ± 60		Gro-1097	6150 ± 60

In all cases where the pollen diagrams gave a well defined assignment to a typical climate (for example, Bölling, Allerød), the dates turned out to be synchronous with the corresponding periods in northwestern Europe and North America.

*Guiana shelf* (South America). In connection with sedimentological studies, a number of carbonate samples (shells, foraminifera, and so forth) from the Western Guiana shelf were dated. They were submitted by D. J. G. Nota, Wageningen. Further details are being published (8).

Station DN 1079, surface.	Gro-462	12,165 ± 350
Station DW 1153, surface.	Gro-473	11,560 ± 240
Station DI 1055, 0.10 to 0.50 m.	Gro-697	5600 ± 150
Station DI 1055, 0.90 to 1.30 m.	Gro-693	5630 ± 160
Station DI 1055, 1.80 to 1.90 m.	Gro-691	6400 ± 145
Station DI 1047, 0.15 to 0.25 m.	Gro-692	14,220 ± 350
Station DI 1047, 0.65 to 0.75 m.	Gro-981	17,550 ± 110
Station DO 1089, 0.30 to 0.60 m.	Gro-985	3400 ± 50
Station DO 1089, 1.40 to 1.60 m.	Gro-991	5980 ± 60
Station DV 1147, 0.40 to 0.80 m.	Gro-984	3210 ± 75
Station DV 1147, 2.50 to 2.80 m.	Gro-982	5075 ± 60

Samples DN 1079 (depth 103 m) and DW 1153 (depth 135 m) consist of calcareous reef material from the shelf rim. Apparently, the reef formation took place in the Pleistocene, when the sea level was about 73 m lower than at present.

Samples DI 1055 were investigated to determine the mean age of the *Amphistegina lessonii* association which at

Description	Sample No.	Age
present is found between 65 and 90 m. Part of this fauna is corroded. In view also of the fact that <i>Amphistegina</i> generally occurs in shallower water, it is supposed that a mixture of recent and subrecent specimens is present. The C <sup>14</sup> dates are in agreement with this assumption.		
Samples DI 1047 are rather old, probably because of redeposition of Pleistocene reefs. The sounding lead yielded indications in this direction.		
Samples DO 1089 and DV 1147 were investigated to determine whether at the present sea level reworking of sandy material takes place. This presumption is proved by the radiocarbon dates, since even at a depth of 2.50 m the age of the shells is not more than about 5000 yr.		
<i>Maas en Waal</i> (province of Gelderland). Four samples from a standard peat section in the Land van Maas en Waal. The pollen diagram was prepared by F. Florschütz. Submitted by L. J. Pons, Bennekom.		
LOG a, Early Subboreal.	Gro-666	4400 ± 120
LOG ba, Early Atlantic.	Gro-662	6850 ± 130
LOG c, Boreal.	Gro-661	8785 ± 160
LOG d, Preboreal.	Gro-665	9825 ± 200
The dates agree with radiocarbon dates from the same pollen zones from other standard sections in northwestern Europe.		
<i>Zuid Holland</i> (Netherlands). Peat lenses occurring below old sea clay (oude blauwe zeeklei) at several places in the province of Zuid Holland. Pollen analysis points to an Atlantic age.		
Berkel, depth 5.50 to 6.00 m, O.D. (ordnance datum).	Gro-1122	5280 ± 90
Nootdorp, depth 5.50 to 6.00 m, O.D.	Gro-1119	5360 ± 70
Boskoop, depth 2.00 m below the surface (5.00 m, O.D.).	Gro-1013	5760 ± 60
Not indicated, depth 0.70 m below the surface.	Gro-1116	4090 ± 55
Apart from the last sample, which might have been contaminated by recent roots, the dates confirm the pollen analytical determinations.		
<i>Vinkeveen</i> (province of Utrecht). Three samples from a standard peat section near Vinkeveen, submitted by J. Bennema, Bennekom.		
End of quercetum mixtum dominance (depth 1.25 to 1.30 m).	Gro-978	4200 ± 80
Beginning quercetum mixtum dominance after <i>Alnus</i> dominance; at the same time, first influence of the "oude zeeklei" (old sea clay) in the profile. Age expected about 4000 B.C. (depth 1.80 to 1.90 m).	Gro-988	5150 ± 65
Intersection of <i>Pinus</i> and <i>Alnus</i> curves. Age expected 5500 B.C. (depth 2.73 to 2.83 m).	Gro-980	5890 ± 60
Three samples from another profile in the same peat section. Submitted by J. Bennema, Bennekom.		
Oligotrophic peat, sub-Atlantic (depth 0.80 to 0.90 m).	Gro-1014	2010 ± 50
<i>Carex-Phragmites</i> peat, sub-Atlantic (depth 1.35 to 1.45 m).	Gro-1015	2075 ± 75
<i>Carex-Phragmites</i> peat, beginning <i>Fagus</i> curve, Subboreal (depth 3.20 to 3.30 m).	Gro-1009	2855 ± 60
The second series of dates is according to expectation. The dates from the		

first series are younger than was anticipated on the basis of pollen analysis by Florschütz. This deviation was suggested to be due to downward transport of humus, but according to our experience this is improbable in this case.

*Houten* (province of Utrecht). Well preserved leaves included in a laminated sand at a depth of 3.00 m. The sand fills a Rhine delta gully, and was inhabited in Roman times. The leaves would date the formation of the gully, which was thought to take place between 1000 and 500 B.C. Collected by K. J. Hoeksema, Bennekom. This result implies that between 3200 B.P. and Roman times the gully was filled up again with about 2 m of deposits. This is considered reasonable.

*Beerta* (province of Groningen). *Phragmites* peat, immediately above and below a heavy decalcified clay, containing *Phragmites* roots, at a depth of 2.20 to 2.90 m below O.D., at Kloostergare near Beerta. This clay could date either from the Boreal-Atlantic transition or from a later period. Collected and submitted by L. A. H. de Smet, Winschoten.

Top sample.

Bottom sample.

The dates indicate that the clay was deposited in the early sub-Atlantic.

*Rauwerd* (province of Friesland). Top of sedge peat containing some clay at a depth of 2.70 to 2.80 m below the surface, underlying sediments from the pre-Roman sub-Atlantic transgression phase, which in the western part of the Netherlands is dated at about 300 B.C. Submitted by J. Cnossen, Heerenveen. The date is according to expectation and confirms the supposed contemporaneity of the pre-Roman transgression phase.

*Takoradi* (Ghana). Mangrove wood from a fossil forest, exposed below high-water mark, lying on the surface of continental deposits, which were flooded by the second Holocene transgression. This transgression has recently been recognized at a number of places along the African coast. In the continental deposits artefacts occurred from the end of the Middle Stone Age. Submitted by O. Davies, University College, Achimota.

*Zwartemeer* (province of Drenthe). Two samples from the upper sub-Atlantic part of the large, raised bog in the southeastern part of Drenthe near Zwartemeer. They were taken to complete the Emmen standard diagram from the same raised bog, described in the previous list (2), in which the sub-Atlantic period was practically lacking, owing to buckwheat cultures.

Depth -0.50. Considerable increase of *Carpinus* (from 3 to 8 percent).

Depth -1.15. First small increase of *Carpinus* (from 0.2 to 1.0 percent).

A more considerable part of the sub-Atlantic peat had been removed by the buckwheat cultures than was anticipated. Although the dates are a valuable addition to the Emmen ones, the middle and upper part of the sub-Atlantic period remains to be investigated.

Gro-1010 3200 ± 50

Gro-1163 2305 ± 65

Gro-1164 2910 ± 60

Gro-1167 2200 ± 65

Gro-1194 5570 ± 70

Gro-1168 1440 ± 40

Gro-1170 2025 ± 70



Table 2. Archeological samples (Europe). All ages are given in radiocarbon years before the present.

Description	Sample No.	Age	Description	Sample No.	Age
<i>Salzofenhöhle</i> (Totengebirge, Austria). Charcoal collected by K. Ehrenberg, Vienna, in the famous Salzofen cave. The problem in this cave is whether the presence of large numbers of skulls and other bones of <i>Ursus spelaeus</i> is due to human activity (9). It is supposed on paleontological and paleobotanical evidence that the habitation took place in an interstadial period. The sample was submitted by A. Bohmers, Groningen. The quantity of charcoal was not sufficient for the larger counter. The present date fully confirms the Pleistocene age of the cave contents.	Gro-761	34,000 ± 3000	140, 6200 ± 150) however, do not differ very much from those of Geleen. Apparently, these settlements lasted for only a few hundred years, and the whole typological evolution took place within that period.		
<i>Lascaux</i> (France). To solve the problem of the age of the famous paintings in the Lascaux cave, a number of samples were collected by A. Glory, Strasbourg, which were directly correlated with archeological remains. So far, only two samples have been measured: charcoal in a hydrocalcite layer on top of a human femur at the entrance of the cave (C), and charcoal with "palettes de couleurs" (B), originating from the "passage."			<i>Hekelingen</i> (province of South Holland). Animal bones from the Neolithic settlement of Hekelingen (12), from which, in the previous list (2), charcoal had been dated at 4200 ± 120 (Gro-254). Submitted by P. J. R. Modderman, Amersfoort. There is no significant difference between bone and charcoal.	Gro-684	4080 ± 85
Sample C.	Gro-1182	8270 ± 100	<i>Chalain</i> (Jura, France). In the neighborhood of the Lac de Chalain in the French Jura two sites were excavated in 1955 by F. Bourdier, Musée National d'Histoire Naturelle, Paris, who collected a number of samples, which were submitted by Florschütz.		
Sample B.	Gro-1514	8060 ± 75	<i>Site Escalon</i> (Ilot des roseaux). At least four superposed archeological levels within lake marl. The samples consisted of wood from the culture layers.		
The recent findings of leaf impressions of <i>Corylus</i> and <i>Quercus</i> in layer C agree with the date obtained. The present dates have apparently no relation to the older paintings; they merely show that the cave was still inhabited in the Mesolithic period. The investigations are being continued.			Layer 3 (-1.10 m) with pottery of Horgen type.	Gro-949	4100 ± 60
<i>Mesolithic samples from the Netherlands</i> . Charcoal from Mesolithic fireplaces (10) of the same kind as described in the previous report (2) from Haule and Waskemeer. These fireplaces are usually found at places of dense flint concentrations on coversand ridges near bogs or brook valleys. Submitted by A. Bohmers, Biological Archaeological Institute, State University, Groningen.			Layer 5 (-1.34 m) with pottery of the same type.	Gro-670	4090 ± 115
<i>Duurswoude I</i> (province of Friesland).	Gro-1173	7460 ± 100	Layer 9 (-1.75 m) with uncharacteristic pottery.	Gro-950	4265 ± 80
<i>Duurswoude III</i> .	Gro-1175	7470 ± 70	Layer 12 (-2.25 m) with pottery of clear Cortaillod type.	Gro-672	4180 ± 130
<i>Een I</i> (province of Drenthe).	Gro-1505	7560 ± 110	<i>Site Bailloud</i> (Vernois sud). One archeological level, dated by Late Bronze Age pottery (Bronze IV, according to Dechelette). The sample was taken from a wooden plank, belonging to the habitation floor. The dates agree with expectation; pollen diagrams are being prepared by Florschütz.	Gro-970	4350 ± 80
<i>Een II</i> .	Gro-1508	7485 ± 100	<i>Nieuw Dordrecht</i> (province of Drenthe). Wood from a trackway (13), which according to pollen analysis would be of late Neolithic age.	Gro-671	2860 ± 80
<i>Siegerswoude</i> (province of Friesland).	Gro-1509	7720 ± 70	<i>Valthe</i> (province of Drenthe). Wood from the famous trackway "Valtherbrug" (14), the age of which has been much discussed. The Neolithic age of the trackway of Nieuw Dordrecht is fully confirmed by the C <sup>14</sup> analysis. The Valthe trackway is obviously much younger. The samples were submitted by W. van Zeist, Biological Archaeological Institute, Groningen.	Gro-683	2985 ± 100
<i>Oirschotse heide</i> (province of N. Brabant).	Gro-1510	7270 ± 60	<i>den Treek</i> (municipality of Leusden, province of Utrecht).		
<i>Drouwen</i> (province of Drenthe).	Gro-1513	7635 ± 90	Charred beam placed above a Drakenstein urn in tumulus 1 at den Treek, municipality of Leusden (15). Submitted by P. J. R. Modderman, Amersfoort.	Gro-1087	3840 ± 55
<i>de Leyen</i> (province of Friesland). Charred <i>Corylus</i> nuts from the culture layer of the Mesolithic site of de Leyen.	Gro-685	6960 ± 140	Charcoal which most probably is contemporaneous with a cremation interment in a coffin in tumulus 2 at den Treek.	Gro-1085	2055 ± 50
Apart from the last one, which has a very different flint typology, all the sites, including Haule and Waskemeer, appear to date from the Boreal period.				Gro-968	3090 ± 70
<i>Geleen</i> (province of Limburg). Two charcoal samples from the early Danubian site (ältere Linearbandkeramik) of Geleen (11).				Gro-971	3300 ± 75
Pit H 11.	Gro-995	6130 ± 60			
Nr 838.	Gro-996	5935 ± 60			
The dates fully agree with those obtained from other Danubian sites. On the basis of pottery typology, Geleen should be somewhat earlier than the greater part of the nearby Sittard site (2). The dates from Sittard (5790 ± 190, 6100 ±					

Description	Sample No.	Age
tumulus 1 (Gro-1051, age 3240 ± 65 yr).		
<i>Halve Mijl-Toterfout</i> (municipality of Veldhoven, province of Noord Brabant). A series of charcoal samples from the Bronze Age necropole of Halve Mijl-Toterfout from which three determinations were published in the first list of dates (1). As no Gro- numbers were added at that time, they are included in the present list. For the location of the samples and so forth, see Glasbergen (16). The samples are also of importance for checking the relative chronology of the barrows as suggested by Waterbolk's pollen analysis. Therefore, they are arranged according to the pollen chronology.		
Tumulus 4, sample 87.	Gro-066	3375 ± 200
Tumulus 1 <sup>B1</sup> , sample 74a.	Gro-050	3450 ± 100
Tumulus 1 <sup>B2</sup> , sample 65b.	Gro-1053	3340 ± 130
Tumulus 1, sample 1e.	Gro-1051	3240 ± 65
Tumulus 5, sample 42.	Gro-1003	3060 ± 50
	Gro-989	3070 ± 50
Tumulus 19, sample 16a.	Gro-1025	3055 ± 50
	Gro-1033	2960 ± 50
Tumulus 8, sample 49.	Gro-049	3055 ± 90
Tumulus 8, sample 49.	Gro-990	3010 ± 60
Tumulus 10, sample 51.	Gro-1000	3080 ± 50
Tumulus 9, sample 84.	Gro-1022	3100 ± 50
	Gro-1029	3090 ± 40
Tumulus 15, sample 64.	Gro-1001	3030 ± 60
Tumulus 3, sample 55.	Gro-1024	3160 ± 50
	Gro-1030	3045 ± 50
To this series can be added a sample from Knegsel, tumulus E, also excavated by Glasbergen.		
Tumulus E, sample 6b.	Gro-1028	2850 ± 40
	Gro-1034	2850 ± 40
On the whole, the relative chronology based on pollen analysis is confirmed. On the basis of the grave typology, tumuli 3 and 9 could be somewhat earlier than suggested by pollen analysis. The radiocarbon dates point in the same direction.		
Tumulus E of Knegsel, containing a Drakenstein urn, appears to be younger than is supposed on the basis of pollen analysis. The date, however, is in agreement with that obtained from tumulus 1 of den Treek (see above). The samples were submitted by W. Glasbergen, Groningen.		
<i>Pylos</i> (Greece). Charred beam of palace from Mycenaean times, probably of Nestor. Collected by C. W. Blegen, Cincinnati. Submitted by H. Brunsting, Leiden. The date is according to expectation.	Gro-998	3010 ± 50
<i>Deventer</i> (province of Overijssel). Charcoal from the Early or Middle Bronze Age settlement on the Margijnenen, municipality of Deventer (17). Depth about 1.00 m. The pottery does not allow an exact date for the settlement. Submitted by P. J. R. Modderman, Rijksdienst voor het Oudheidkundig Bodemonderzoek, Amersfoort. The radiocarbon date proves a Middle Bronze Age dating of the settlement.	Gro-955	2820 ± 70
	Gro-967	2890 ± 70
<i>Elst</i> (province of Gelderland). Human skull, which, on anthropological grounds, was thought to be of Pleistocene age. In the neighborhood, mammoth bones have been found. The		

Description	Sample No.	Age
sample was submitted by J. Huizinga, Utrecht.		
Human skull.	Gro-997	2325 ± 75
Mammoth bone.	Gro-712	> 20,000
The skull is obviously of late Holocene age.		
<i>Dorreegeest</i> (municipality of Uitgeest, Noord Holland). Fragment of a wooden harrow, found in a pit at Dorreegeest, excavated by F. C. Bursch. The stratigraphical context is not clear. At the site both medieval and Iron Age remains were found. Submitted by J. M. G. van der Poel, Wageningen. The date proves that the harrow indeed belongs to the earlier habitation phase. It is the oldest harrow so far known.	Gro-1171	1680 ± 60
<i>"Eschböden"</i> (Emsland, Germany). Three charcoal samples collected in the bottom part of "Eschböden," that is, the soil of fields which in the course of centuries has grown in thickness as a result of manuring with turf from sheep stables. The age of the "Esche" is a much discussed problem. Collected and submitted by G. Niemeier, Braunschweig.		
Hesselte.	Gro-1008	1200 ± 45
Ahlen.	Gro-1037	1670 ± 45
Milte.	Gro-1038	1860 ± 50
	Gro-1052	1840 ± 50
The "Esche" appear to be older than generally is believed, and seem to go back as far as the beginning of our era. The date of Milte is in agreement with that of some sherds found in the same layer.		
<i>Wijster</i> (municipality of Beilen, province of Drenthe). Wood from the front wall of an Anglo-Saxon hut (18). A date of A.D. 400 was expected on the basis of the presence of sherds of a late Roman glass bowl in the filling of the hut. Submitted by H. T. Waterbolk, Groningen. The date (18a) is somewhat younger than was expected, but there is no real proof that the sherds are contemporaneous with the hut. They surely got in the hut after it had collapsed, but they may have been lying in the soil, which originally formed the side walls of the hut. There are traces of earlier habitation at the site.	Gro-1176	1315 ± 40
<i>"Roodzand."</i> Fairly frequently a typical red sand (roodzand) is found on the Veluwe (province of Gelderland). The origin of this red sand has been a subject of many speculations. One theory, which is supported by the present dating of charcoal found in the sand, correlates it with charcoal production for iron foundries, of which many remains have been found and which have been dated in about the 8th century (18a). The sample was submitted by G. Maarleveld.	Gro-1103	1100 ± 65
<i>Ghent</i> (Belgium). Wooden structure below the "Gravensteen," on archeological evidence supposed to be of Viking age. The presence of Vikings in Ghent from 879-881 is a historical fact. A second wooden building below the Gravensteen dates from about A.D. 1035. Submitted by E. G. Boers, Ghent. The date (A.D. 1016 ± 50) does not agree with the assumption that the building was erected by the Vikings; it agrees with the age of the second building (18a).	Gro-1046	940 ± 50

Description	Sample No.	Age
<i>Karolingian Chapel</i> (Nijmegen, province of Gelderland). In view of a controversy as to the age and building history of the tuff part of the so-called Karolingian Chapel, a number of corresponding wood samples were dated. Gro-976 and Gro-1502 were submitted by J. G. Deur, Nijmegen; Gro-977, by H. Brunsting, Leiden.		
Beam from upper part of central pillar structure.	Gro-976	760 ± 40
Beam from lower part of central pillar structure.	Gro-1502	900 ± 40
Other beam, belonging to the same early part of the building.	Gro-977	900 ± 45
According to these dates, there is indeed a difference in age between parts of the central structure. However, the earlier part does not appear to go back to Carolingian times (18a). There are also architectural arguments in favor of a date in the first half of the 11th century A.D.		

Description	Sample No.	Age
<i>Rijnsburg</i> (province of South Holland). Two skeletons from a group of graves found during the excavation of the Abbey of Rijnsburg. The first was thought to be that of Floris V, Count of Holland, who was murdered in 1296. The second is from a skeleton lying close to the former. Submitted by W. Glasbergen and B. K. S. Dijkstra, Groningen.		
I.	Gro-677	945 ± 100
	Gro-680	900 ± 70
	Gro-1111	970 ± 40
II.		
The dates are systematically somewhat too old; a more detailed investigation into the possibilities of errors with dating of bones is planned, including a calibration with more recent bones (18a).		
<i>Bargen</i> (Schaffhausen, Switzerland). Charcoal from medieval (14th century) iron melting oven. Submitted by W. Guyan, Schaffhausen. The date agrees with the expectation.	Gro-1005	640 ± 50
	Gro-1020	660 ± 45

Table 3. Archeological samples (Asia, Africa, America).

Description	Sample No.	Age
<i>Niah Caves</i> (West Sarawak, British Borneo). Charcoal samples reflecting tools supposed on archeological grounds to be Middle Stone Age type (unworked stone and pebbles, bone points, animal remains and shell in bulk, quartz pebble fire strikes and charcoal). The first sample (Gro-1159) represents the upper limit of "flake" and "blade" concentration. The second sample (Gro-1158) represents the bottom of the same layer (depth about 1 m). The third sample came from a depth of 2.5 m but from a different location. Archeologically it is somewhat older than the second sample. The deposits continue several meters below the third sample, but are not yet fully analyzed. The results are older than hitherto expected, but they agree with the ideas of the submitter of the sample (19). This is the first Paleolithic settlement discovered in this part of the world. The samples were collected by M. W. F. Tweedie, director of the Raffles Museum, Singapore, and T. Harrison, curator of the Sarawak Museum, during excavations by the Sarawak Museum.		
	Gro-1159	19,570 ± 190
	Gro-1158	32,630 ± 700
	Gro-1338	41,500 ± 1000
<i>Jericho</i> (Palestine). Charcoal of Tamarisk from the late pre-pottery Neolithic phase (Layer Y, Square F1). Supplied by F. E. Zeuner, London.		
	Gro-942	8900 ± 70
	Gro-963	8785 ± 100
Zeuner, using a pretreatment with acid only, had obtained (F-38) 7800 ± 160 yr but after an alkali treatment, 8670 ± 200 yr (F-41) was found. When using the same pretreatment, both laboratories thus produce the same figures.		
<i>Egypt</i> . Wood from the First Dynasty tomb of Waji (or Zet) in the necropole at Saqqara, excavated by Emery. It should be about a generation older than the grave of Den (see previous list, 2), which has produced a date of 4450 ± 100 yr (Gro-689). Supplied by H. Barker, the British Museum, London.		
	Gro-1100	4120 ± 60
	Gro-1109	4220 ± 55
Wood from the deck of the funerary ship of Sesostri III. Expected age 3750 yr.		
	Gro-1157	3310 ± 55
	Gro-1178	3370 ± 50

Description	Sample No.	Age
Section of a tree trunk from the pyramid of King Mentuhotep II or III at Dier at Bakri (Thebes). The date of death of this king, irrespective of whether he was Mentuhotep II or III, is reckoned to be about 2010 B.C. This date is based on astronomical evidence. The probable error should not be more than 20 yr.		
	Gro-1155	3420 ± 55
	Gro-1177	3420 ± 55
All the samples came out much younger than was expected. The same was the case for samples from the previous list. The discrepancy is only partially due to isotopic fractionation in the sample. The difference in the C <sup>13</sup> /C <sup>12</sup> ratio between the calibration sample and the present two samples was 0.5 percent only. So 80 yr have to be added to the ages given. The sample from Sesostri III was also dated by Libby, who got (C-81) 3621 ± 180 yr. Our sample was a part of the same piece of wood.		
<i>Fimnah</i> (Israel). Charcoal from a grave in the Wadi Fimnah acropolis in the Negeb Desert. The date is of importance for the history of mining in the area. Both copper and iron were produced at the site (20). The sample was submitted by V. P. Sokoloff, Haifa.	Gro-938	2655 ± 65
<i>Wadi Muraba'at</i> (Jordan). Woolen textile from one of the caves associated with the famous Dead Sea Scrolls. The expected age is approximately 1800 yr (Bar Kochbak's revolt) on archeological evidence. Supplied by F. E. Zeuner, London. With acid treatment only, Zeuner found (F-37) 1350 ± 60 yr. In this case also, the difference is probably due to the pretreatment applied.		
	Gro-940	1665 ± 42
	Gro-943	1575 ± 50
	Gro-965	1550 ± 75
<i>Gran Canario</i> . Six samples relating to the fair, blue-eyed people (Guanches), who lived on the Canary Islands before the arrival of the Spaniards. They show anthropological characters of the Cro-Magnon type. Apart from the last sample, the material consists of mummy skins and woody material covering		

Description	Sample No.	Age
mummies, which were buried in caves. Submitted by C. R. Gavilanes, Las Palmas.		
Guayadeque, wood.	Gro-1190	980 ± 60
Guayadeque, mummy skin.	Gro-1189	1170 ± 60
Acusa, wood.	Gro-1127	1280 ± 45
Acusa, mummy skin.	Gro-1188	1140 ± 60
Guevas del Rey, wood.	Gro-1191	1420 ± 60
Galdar, wood from a sepulchral monument.	Gro-1192	635 ± 60

The dates, though rather late, are perfectly acceptable. There is no significant difference between the mummy skin and the wood at the first two sites.

Description	Sample No.	Age
Mayapan (Yucatan, Mexico). Charcoal from burned beam on floor of structure R-87, Mayapan, Mexico. Expected age 500 yr. The specimen should date the approximate termination of the Mayan civilization. The sample was submitted by H. E. D. Pollock, Carnegie Institution of Washington, Cambridge, Mass. There is an upper limit on historical evidence of approximately A.D. 1540 for the ruin of Mayapan. A correction of 100 or 200 yr for the Suess effect would bring the C <sup>14</sup> date in accord with the archeological evidence.	Gro-1166	400 ± 55

Table 4. Special problems.

Description	Sample No.	Age
Klazienaveen (province of Drenthe). Layer of peat on sand, containing three infiltration bands of humus. The stratigraphy was as follows: Peat up to a depth of 40 cm. At 60 cm the first humus band. At 130 cm a white band in the sand, typical for the Allerød in this region. At a depth of 180 cm the second humus band. At 210 cm the third band. The three layers contained about 5, 1.2, and 1.2 percent of humus, respectively. It was collected by washing the sand with water until it was clear. The water was then centrifuged. For the second band, it was checked that the material obtained was completely soluble in alkali. The samples were collected and submitted by B. van Heuveln.		
Bottom of peat.	Gro-1019	3230 ± 75
First layer.	Gro-1016	2090 ± 50
Second layer.	Gro-710	1535 ± 85
Third layer.	Gro-711	2550 ± 100

Description	Sample No.	Age
It is obvious that humus passed through the peat and perhaps even through humus layers deposited earlier, though it is also possible that the lower layers were produced first. The results are of interest for studies of humus transports in the soil, as well as for discussions of possible errors in C <sup>14</sup> datings, introduced by infiltration of more recent material. The date of the peat agreed with the pollen analysis (Subboreal).		
Storbreen glacier (Norway). By a special apparatus, CO <sub>2</sub> was collected from about 6 tons of ice by Coachman <i>et al.</i> The sample contained about 0.3 g of carbon. The date is in excellent agreement with the estimates made by the Norsk Polarinstitut. A more detailed discussion can be found in (21). The main aim of the present measurement was to prove the feasibility of the procedure; further investigations are planned.	Gro-758	710 ± 120

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## S. R. Gevorkiantz, Forest Biometrician

Suren R. Gevorkiantz, mathematical statistician at the Lake States Forest Experiment Station and internationally known research forester, died on 8 May 1958, after collapsing at work. Thus a still productive career was brought to a sudden close.

Gevorkiantz was born in Tiflis in the Russian Caucasus on 27 July 1899. He was brought up, however, in the Baikal region of Siberia, where he attended the Government Classical Gymnasium at Chita from 1908 to 1917. He began collegiate work in mechanical engineering in 1917 at the Imperial Institute of Technology in Tomsk, Siberia. In 1918 the Russian Revolution cut short his educational pursuits, and near its conclusion, in 1919 Gevorkiantz fled to northern China. For the next 3 years, he was a refugee in China, Manchuria, and Japan. From the latter country he made his way to California in 1922. There he entered the Forest School and obtained his B.S. degree from the University of California in 1924. Later he attended the Harvard Forest School where he obtained the M.F. degree in 1928.

In January 1925 Gevorkiantz became a member of the staff of the Lake States Forest Experiment Station, Forest Service, U.S. Department of Agriculture, on the St. Paul campus of the University of Minnesota. He was attracted there by the fact that another former refugee from Russia, Raphael Zon, was director of the station. Gevorkiantz continued at the station until his death. Although his entire career was spent in one locality, he became widely known both nationally and internationally. His research was confined largely to the fields of forest mensuration and the application of statistical methods to forestry and related problems. His work has been reported in more than 100 publications of which he is author or coauthor.

Gevorkiantz' professional accomplishments were numerous and substantial. In forest mensuration he developed

original volume and yield tables for the principal species and forest types in the Lake States; two of them involved the development of original procedures. He devised methods for predicting forest growth under various conditions, including the difficult situation in uneven-aged stands. He developed composite volume tables that can be applied regardless of species. He defined a large proportion of the mensurational and statistical terms used, in *Forestry Terminology, A Glossary of Technical Terms Used in Forestry* (Society of American Foresters, Washington, D.C., ed. 3, 1958).

In the application of statistical methods to research problems he made an outstanding contribution. His advice in designing scientific experiments was sought and applied not only by members of his own organization but also by members of other federal, state, and private agencies in forestry, entomology, genetics, plant pathology, wood utilization, and wildlife management. He was called upon to present papers in this field at national meetings.

The simplified techniques that he stressed made it possible for practising foresters to understand and make better use of statistical methods. He developed rules of thumb (with a mathematical basis) for log scaling. He derived a method of sample scaling for national forest timber sales and for estimating stand volume directly in the field. He was joint author of a timber-cruising manual widely used by timber estimators, teachers, and students [J. W. Girard and S. R. Gevorkiantz, "Timber Cruising" (U.S. Forest Service) (Processed)]. His cumulative volume tally sheet is widely used in the Lake States and other regions.

Gevorkiantz was active in several professional societies. He was a long-time member of the American Association for the Advancement of Science and of the American Statistical Association. During his 30 years in the Society of American Foresters he served three times as a sec-

tion officer and was associate editor of the *Journal of Forestry* from 1946 to 1957. In the latter capacity he set and upheld high standards for articles on forest mensuration and statistics appearing in the *Journal*.

Few are as versatile as Gevorkiantz was. Aside from his excellence in mathematics and forestry, he was an interesting speaker, a good teacher, an entertaining and stimulating conversationalist, an accomplished artist, an untrained but skillful musician, and an enthusiastic performer in such sports as golf and bowling. He was basically an optimist, and everything he undertook from the simplest to the most complex activity, was an adventure.

Gevorkiantz was an unusually considerate person. Coupled with this was remarkable patience. These two attributes were most evident when he was helping other workers design experiments or select methods for analyzing data. He would spend a great deal of time, where necessary, first in understanding the problems that confronted the worker and then in searching out or devising methods or procedures that best suited the individual cases. The evident confidence with which he approached these problems, along with the high degree of success that attended his efforts, in turn inspired great confidence in those who consulted him.

In recent years Gevorkiantz received some tangible recognition for his professional accomplishments. In 1953 he received the Superior Service award of the U.S. Department of Agriculture, and in 1957 he was elected fellow of the Society of American Foresters. He thoroughly enjoyed these honors, but he appeared to derive even greater satisfaction from the esteem in which he was held by his friends and associates. He was respected by many, ranging from such giants in research as Sir Ronald A. Fisher to the youngest neophytes. So far as his associates knew, he was truly a man without an enemy.

Gevorkiantz' passing leaves an unfilled void in the profession. To his family, friends, and associates it leaves a personal sense of loss alleviated only by memories of this warm, helpful, and talented person and his accomplishments.

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# News of Science

## International Council of Scientific Unions

Between the second and the sixth of October there was held in Washington a session of the highest significance to the international scientific community. This was the eighth triennial General Assembly of the International Council of Scientific Unions, widely known as ICSU, which met at the National Academy of Sciences-National Research Council. Lloyd V. Berkner, president of the International Council, presided.

At the opening session of the assembly on 2 October, Detlev W. Bronk, president of the National Academy of Sciences, welcomed the delegates and congratulated ICSU on its signal success in furthering international cooperation among the scientists of the world. He spoke of the International Geophysical Year (IGY) as one example among many of the important activities going forward under ICSU sponsorship. He noted with appreciation that several of the significant research programs initiated as part of the IGY would be continued. Following Bronk's remarks, Berkner delivered his presidential address, and the secretary-general and the treasurer presented their reports. Succeeding sessions of the assembly were devoted to consideration of items on the agenda. Special events included an evening reception tendered by the Deputy Under Secretary of State and Mrs. Robert Murphy, a reception and buffet supper by the President of the National Academy of Sciences and Mrs. Bronk, tours of scientific laboratories in the Washington area, and an all-day excursion to the Blue Ridge Mountains of Virginia on Sunday, 5 October.

Well over 100 delegates participated in the assembly, representing all 13 of the member scientific unions and 30 of the 45 adhering countries. The United States was represented by the following delegation: Detlev W. Bronk, honorary chairman; W. Albert Noyes, Jr., chairman; Wallace W. Atwood, Jr., secretary; Wallace R. Brode, Ralph E. Cleland, Hugh L. Dryden, A. Baird Hastings, Joseph Kaplan, Otto Struve, and Alan T. Waterman.

It was especially fitting that the National Academy of Sciences be host to this assembly, because the academy serves as the adhering organization for the United States, sponsoring national committees for each of the constituent international unions and coordinating their activities through the academy's Office of International Relations.

### Organization of ICSU

Nearly all scientists have heard of ICSU and many thousands of them have participated in the work of one or more of ICSU's member unions, joint commissions, or special committees. However, very few scientists, numerically, are familiar with the organizational structure of ICSU. For this reason it may be useful to describe briefly the pattern of organization which makes ICSU unique among international councils and which has brought to ICSU the responsibility of initiating and carrying through important scientific programs requiring international cooperation.

The basic organizational structure of ICSU was adopted in 1931 when the International Research Council, which had been in existence since the close of World War I, was reconstituted as ICSU. Since that time, a few minor changes have been introduced, but the fundamental features of the ICSU organization have remained unchanged. Figure 1 shows the present pattern.

The strength of ICSU is found in its two categories of membership—scientific members and national members. The scientific members are autonomous international unions, each concerned with a particular scientific discipline; the national members are normally the leading academies of sciences or research councils in the countries concerned. The role of ICSU is that of a coordinating body. It does not direct the activities of its member unions. The bureau, executive board, and assembly are the administrative bodies of the organization.

In furthering international scientific research, ICSU relies upon its member unions and its national adhering organizations. Relations with governments are arranged through the academies and research councils which serve as the na-

tional adhering organizations. In this manner ICSU has obtained the assistance of governments in the furtherance of important scientific investigations.

Best known of ICSU's activities is the International Geophysical Year. Scientists and laymen alike are familiar with this vast international cooperative research operation. They know that the exploration of Antarctica by scientists of 12 nations is part of the IGY and that the instrumented earth satellites now circling the earth are IGY vehicles gathering data for the scientists of the world.

During the last 10 years, ICSU has received substantial support from UNESCO. This support, amounting to nearly \$200,000 annually, has helped ICSU and its member unions to reestablish themselves following World War II and to greatly extend their important cooperative programs. A formal agreement between ICSU and UNESCO provides for a continuing relationship wherein mutual assistance is assured. This agreement contributes significantly to the work of both organizations.

In addition to the support mentioned above, ICSU and its unions receive special contributions from foundations and from national adhering academies. In recent years support from these sources has increased substantially.

### General Assembly Actions

In the succeeding paragraphs the more significant actions taken by the delegates to the Eighth General Assembly of ICSU are recorded. These include adoption of a policy statement reaffirming the purely scientific character of ICSU, establishment of new committees and services to carry forward important international cooperative research programs, launching of a quarterly journal, and actions on a number of administrative and financial matters.

**Political nondiscrimination.** Because of the many problems of a political or jurisdictional nature which have appeared on the horizon to hamper travel of scientists and their participation in international activities, the assembly delegates believed it necessary to reaffirm the purely scientific character of ICSU. Accordingly they approved the following statement:

"To ensure the uniform observance of its basic policy of political non-discrimination, the ICSU affirms the right of the scientists of any country or territory to adhere to or to associate with international scientific activity without regard to race, religion or political philosophy.

"Such adherence or association has no implications with respect to recognition of the government of the country or the territory concerned.

"Subject only to payment of subscriptions and submission of required reports,

the ICSU is prepared to recognize the academy, research council, national committee, or other bona fide scientific group representing scientific activity of any country or territory acting under a government de facto or de jure that controls it.

"Meetings or assemblies of ICSU or of its dependent organisms such as its special committees and its joint commissions should be held in countries which permit participation of the representatives of every national member of ICSU or of the dependent organisms of ICSU concerned, and allow free and prompt dissemination of information related to such meetings.

"ICSU and its dependent organisms will take all necessary steps to achieve adherence to these principles."

**Collaboration in geophysics.** The International Geophysical Year has provided an outstanding example of the accomplishments made possible by ICSU procedure under which each country plans, through its own academy or other national scientific organization, its research program; and ICSU through its special committees arranges the coordination of efforts, simultaneously assur-

ing insofar as possible that gaps do not occur in the program.

Thus, for example, in the preparation of antarctic weather maps so vital to all antarctic operations, American and Russian scientists and those of other nationalities have been enabled to work in harmony. Similarly, all the observations and discoveries of the IGY are made available through world data centers in the U.S.S.R., in Western Europe, and in the United States.

With the observation stage of the IGY due to end on 31 December 1958 and with the Special Committee for the IGY going out of existence on 30 June next, the assembly took positive steps to guarantee continuance of international geophysical collaboration and of the work begun under the IGY. It provided for a successor group called the Special Committee for Inter-Union Cooperation in Geophysics, to be known as SCG, which will begin functioning as soon as the Special Committee for the IGY ceases. There will thus be on hand a unit commissioned to deal with the varied aspects of the closing stages of the IGY. Among its activities will be the publication—largely in the *Annals* of the IGY—of the

data collected during the 18 months of IGY observations. The SCG will also undertake to organize thoroughgoing cooperation on the international level in the use and analysis of these data through the World Data Centers, the International Scientific Unions, and the World Meteorological Organization, and in any other way suited to this purpose.

**Oceanic research.** There was established a Special Committee on Oceanic Research, to be known as SCOR. This body is charged with furthering the coordination of scientific activity in all branches of oceanic research, with a view to framing a scientific program of worldwide scope and significance.

**Antarctic research.** A Special Committee on Antarctic Research was also established, to be known as SCAR, for the stated purpose of furthering the coordination of scientific activity in Antarctica.

**International Service for World Days.** Another significant result of the IGY was recognized with the establishment of the International Service for World Days, or IWDS. This service will carry forward the World Days cooperation, which has greatly facilitated simulta-

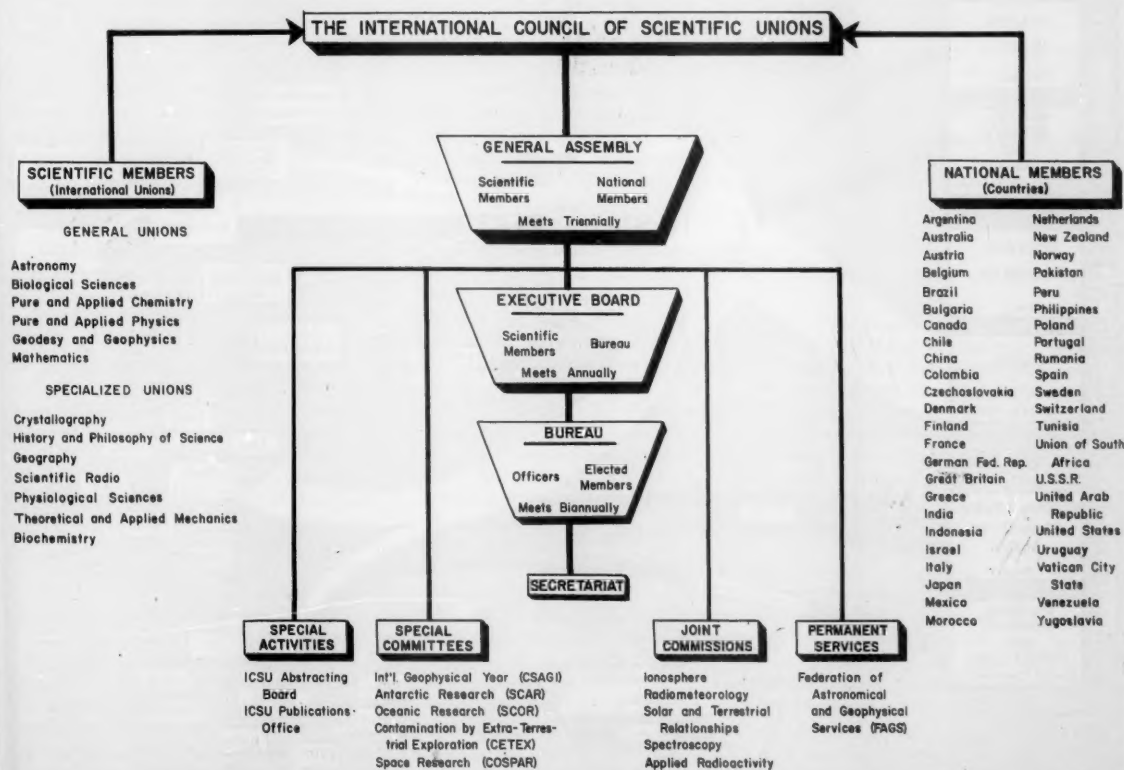


Fig. 1. The organization of ICSU as visualized by the author; no official chart exists. The general assembly is the top administrative body composed of delegates appointed by the scientific and national members. The bureau and executive board conduct the affairs of ICSU between triennial assemblies. The secretariat, with offices at The Hague, consists of the administrative secretary, the accountant, and secretarial assistants.



neous IGY observations of atmospheric and other phenomena at many localities over the globe. In addition to permitting advance planning, the continuance of the IWDS will perpetuate the warning-alert communications system that makes possible simultaneous observations even of phenomena that develop at the last minute.

**Space research.** Recognizing the need for an international committee to deal with problems of space research and considering that the ICSU should continue its work of coordination in this field, the assembly authorized the establishment of a Committee on Space Research, to be known as COSPAR. The assembly specified the terms of reference of the new committee as follows:

"The primary purpose of the Committee is to provide the world scientific community with the means whereby it may exploit the possibilities of satellites and space probes of all kinds for scientific purposes, and exchange the resulting data on a cooperative basis. It shall further report to ICSU these measures

needed in the future to achieve the participation in international programs of space research of all countries of the world with those which are already actively engaged in research programs involving the use of instrumented earth satellites and space probes.

"The Committee shall hold as a primary objective the maximum development of space research programs by the international community of scientists working through the ICSU and its adhering national academies and unions. Recognizing, however, the need for international regulation and control of certain aspects of satellite and space probe programs, the Committee shall keep itself fully informed on United Nations or other international activities in this field, in order to assure that maximum advantage is accorded international space science research through such regulations, and to make recommendations relative to matters of planning and regulation that may affect the optimum program of scientific research."

By this resolution, the assembly sig-

nified the intensity of the hope in the international scientific community that such a committee, or any successor it may have, will in fact be the international scientific body to further space research on the part of all nations; this will guarantee that the goal will always be the free and unhindered expansion of knowledge. The new committee held its first meeting in London in November, less than 6 weeks following the close of the assembly in Washington.

On a related matter, the Committee on Contamination by Extra-Terrestrial Exploration (CETEX) was instructed to draw up a code of conduct for interplanetary exploration and to report its conclusions to the Committee on Space Research [see *Science* 128, 887 (17 Oct. 1958)].

**Freedom of scientific research at sea.** Lest the new Convention on the Continental Shelf, adopted by the United Nations Conference on the Law of the Sea, become a source of possible interference with the freedom of oceanic research, the assembly requested its national members

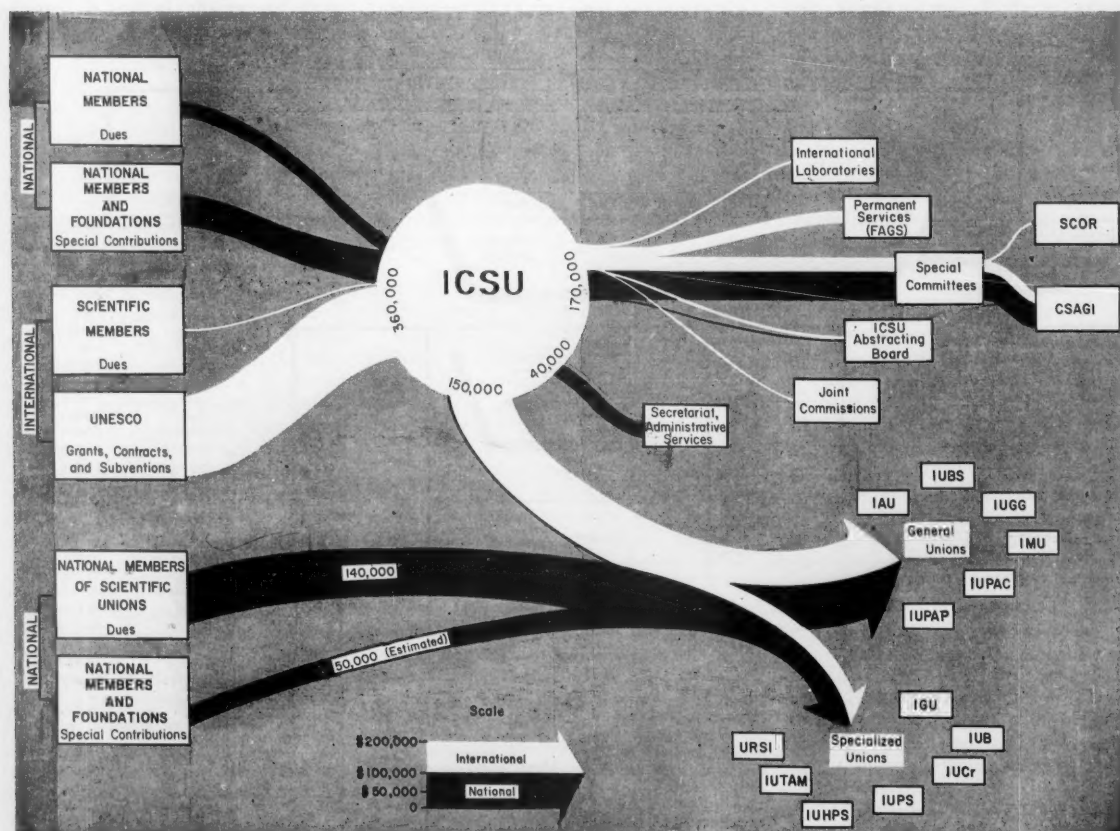


Fig. 2. Flow-chart showing to scale the income and expenditures of ICSU and its member unions in 1957 (all figures are approximate). Over 62 percent of the total income was used for union activities; 30 percent for special committees, permanent services, and related projects; and about 7 percent for secretariat and administrative services. The unions and special committees identified by initials only are named in Fig. 1.



to ask their separate governments, when ratifying the convention, to signify that they therewith grant general permission to any scientific research vessel to conduct investigations of the bottom and subsoil of the continental shelf, provided that the program is specifically approved by ICSU and that the results of the investigations will be published openly for the benefit of science. It was recommended that the coastal state concerned should be notified far enough in advance to enable it, if it so wishes, to designate a representative to take part in the work. In this way, it is hoped that governments will be substantially assisted in identifying bona fide scientific research projects and that diplomatic delays which might jeopardize many types of oceanographic investigations may be avoided.

**Publications.** Starting in 1959 a new quarterly international journal to be known as the *ICSU Review* will be published, to cover all significant activities of ICSU and its member unions; it will also assure the regular appearance of a current bibliography of ICSU publications.

And, because of the special demand stimulated in large measure by the IGY activities, there is to be established a new ICSU Publications Office. Among the several functions of this office will be (i) publication of the *ICSU Review*, (ii) production of a self-consistent series of volumes of high standard in the fields of activity of ICSU and its dependent organisms, (iii) provision of editorial and publication assistance to scientific groups associated with ICSU, and (iv) financing, promotion, and distribution of ICSU publications.

**UNESCO relations.** In recognition of the close and mutually advantageous relationship between ICSU and UNESCO, the assembly expressed its deep appreciation for the latter's significant support of the work of ICSU and its associated scientific unions and noted with pleasure that ICSU programs have, in turn, materially furthered the objectives of UNESCO. The hope was expressed that UNESCO would undertake a major expansion of its Marine Sciences Program and that it would aid the countries bordering the Indian Ocean to take an active part in the international investigation of that ocean planned by SCOR.

It was also urged that scientific members be included in each national delegation to general conferences of UNESCO in order to insure full consideration of the program of the Natural Sciences Department, which in recent years has received a smaller and smaller percentage of the total UNESCO budget.

**Financial matters.** As controller of its own financial affairs, the assembly passed a resolution strongly endorsing the es-

tablishment of a capital fund and instructing the treasurer to invite each council member to take early and vigorous action to secure appropriate donations. Such a fund, preferably aggregating \$1 million, is needed to permit ICSU to meet its steadily growing responsibilities and to move swiftly when significant developments in international science demand immediate and positive action.

At the same time, thanks and appreciation were expressed for contributions totaling some \$28,000 to the ICSU Special Fund made by the Sir Darabji Tata Trust of India, the Academy of Sciences of the U.S.S.R., and the National Academy of Sciences and National Science Foundation of the United States.

Figure 2, prepared by the academy's Office of International Relations, shows the "national" and "international" income of ICSU and its member unions in 1957. It also shows how these funds, approximately \$550,000, were used by ICSU for specific projects, including the IGY, and by the unions for support of their activities. Secretariat and administrative services provided by ICSU amounted to a little over \$40,000.

The assembly approved an annual operating budget of \$58,000 for the next triennium. The allocation of ICSU funds to special projects and to the 13 member unions was reserved for action by the executive board, which meets annually.

**Admission of new national members.** The assembly admitted the National Council of Scientific and Technical Research of Argentina and the Bulgarian Academy of Sciences as new national members of ICSU.

**Election of new bureau.** The following officers and members of the bureau were elected to serve until the next triennial assembly: Sir Rudolph Peters (Great Britain), president; Lloyd V. Berkner (United States), retiring president; Reverend Pere Lejay (France), vice president; W. A. Engelhardt (U.S.S.R.), vice president; Colonel E. Herbays (Belgium), treasurer; Nicolai Herlofson (Sweden), secretary-general; and Arthur Stoll (Switzerland) and Seiji Kaya (Japan), members.

The new bureau lost a valuable member with the passing of Reverend Pere Lejay on 11 October during the return voyage to his homeland.

A special vote of appreciation for valued service to ICSU was extended to retiring members of the bureau: Bertil Lindblad (Sweden), Sir K. S. Krishnan (India), and Sir Harold Spencer Jones (Great Britain).

#### Summary

The preceding account of the Washington assembly of ICSU is for the most part factual. It is essentially a record of actions taken by the assembly. As such,

it summarizes the work of the delegates and reveals the plans, hopes, and aspirations of the international scientific community. The importance of freedom of scientific research from artificial restrictions of any kind, political or otherwise, has been reaffirmed. The important types of research arising out of the highly successful International Geophysical Year will be carried forward on an international basis under ICSU auspices by groups newly constituted for the purpose. The necessity for continued international scientific cooperation, with a maximum of support from such kindred units as UNESCO, has been made clear, as has been the need for adequate funds for the work. New facilities for publication and dissemination of material will provide another step forward in what every scientist trusts is steady progress toward uncompromised, uncompromising, and recognized universality for science and scientific knowledge.

The accomplishments of the IGY have yet to be evaluated, and many another task remains to be completed. But plans already are being made for new and daring explorations into the unknown, always pushing forward the frontiers of knowledge. This is the spirit of ICSU and of all those who together constitute the ICSU family of scientific unions. As ICSU grows, so will our knowledge of nature and our ability to cope with the problems which currently beset the peoples of the world.

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#### Overseas Science Officers

The Department of State has announced the re-establishment of its overseas Science Officer Program with the appointment of seven distinguished scientists to serve in the U.S. embassies in London, Paris, Rome, Bonn, Stockholm, and Tokyo. The men selected are as follows: Thomas H. Osgood, physicist and dean of the School of Advanced Graduate Studies at Michigan State University, for London; Edgar L. Piret, professor of chemical engineering at the University of Minnesota, for Paris; Edward H. Cox, retired head of the department of chemistry at Swarthmore College, as deputy science officer for Paris; Walter Ramberg, chief of the Mechanics Division at the National Bureau of Standards, for Rome; Ludwig F. Audrieth, professor of chemistry at the University of Illinois, for Bonn; Julian E. Mack, professor of physics at the University of Wisconsin, for Stockholm; and Willis R. Boss, professor of zoology at Syracuse University, for Tokyo.

These 2-year appointments constitute the first of a series for the science program, which is under the direction of Wallace R. Brode, science adviser to the Secretary of State. Still to be appointed are science officers for the U.S.S.R., India, and South America, and deputy science officers for all the posts except the one in Paris, to which Cox is being assigned. Leaders in science who have had experience as educators, research scientists, and administrators have been especially selected for these posts because of their international scientific reputation, their knowledge of the status of science and acquaintance with scientists in the country of assignment, and their facility with the language.

A science officer's primary role will be to serve as an adviser to the ambassador and his staff in the evaluation of the interaction of science with foreign policy, the assessment of current scientific progress abroad, and the enhancement of the liaison between U.S. and foreign scientists and engineers. There are 24 countries that have scientific attaches in their embassies in Washington, attesting to the need and usefulness for representation of science in international affairs.

### **Jet Propulsion Laboratory Transferred to NASA**

An executive order was issued by President Eisenhower on 3 December that transfers from the Army to the National Aeronautics and Space Administration the facilities of the California Institute of Technology's Jet Propulsion Laboratory. In addition, NASA and the Department of Defense have agreed that, at NASA's request, the Defense Department will make available a portion of the research and development capacity of the Army Ballistic Missile Agency at Huntsville, Ala. Under the Army-NASA agreement, which accompanied the executive order, Wernher von Braun and his 2900-man space research group will devote part of their activities to peaceful projects for the space agency. This will include eight satellite launchings next year.

The Jet Propulsion Laboratory will continue to be operated by the California Institute of Technology, as contractor for NASA. Under the agreement, which accompanied the executive order, Army projects now underway at JPL will continue under Army supervision until they are "phased out," largely during 1959. These constitute more than half of the research program at JPL and include work on the Sergeant missile and on several smaller, classified projects.

The Jet Propulsion Laboratory was established prior to American participation in World War II. Pioneering work

was performed there on solid propellants for rockets; in addition, JPL scientists are recognized as leaders in electronics, communications, and guidance systems for space technology. The JPL facilities are valued at approximately \$55 million; more than 2300 scientists, engineers, and supporting personnel are employed at this research center.

Discussions between NASA and the Department of Defense over the transfer of facilities began nearly 2 months ago. T. Keith Glennan, NASA administrator, pointed out that NASA, in order to discharge fully its responsibilities as set forth in Public Law 85-568, must develop at the earliest possible moment a capability for the effective handling of the functions connected with the design, development, and use of satellite systems, including propulsion units, guidance and control, scientific payload packages, and the acquisition and analysis of data of interest to both the scientific community and the Department of Defense.

Glennan said that NASA had assigned the highest order of importance to the avoidance of significant interference with the discharge of missions in support of the defense effort assigned to the separate installations by the several services. He estimated that if NASA were to develop its own facilities to perform nonmilitary space projects, an investment of more than \$60 million would be required, and it would be necessary to recruit a scientific and supporting staff of between 2000 and 3000 people. Building and staffing such a complex of space technology facilities would require 3 to 4 years.

Deputy Secretary of Defense Donald A. Quarles, in the course of the discussions, informed Glennan that the Department of Defense agreed that the Army facilities at JPL could be transferred to NASA at once, but that it could not agree to the proposed partial transfer of ABMA to NASA. The reason for the latter decision was that the Army is now engaged in the development of missiles and that the unique capabilities of the ABMA team (Wernher von Braun's group) are essential to vital and high-priority Department of Defense programs for the development of advanced military systems. However, he suggested a portion of the capacity of ABMA could be made available for work on NASA space projects.

Glennan agreed to the Defense Department proposal, saying that for the present it provides a workable solution to NASA needs. Moreover, the NASA administrator observed that every effort will be made to utilize the skills of ABMA to the maximum extent feasible. The Department of Defense and NASA are agreed that within the next year a

joint report will be made to the President and the Space Council about the experience under the cooperative arrangements that have been announced.

### **Project Discoverer**

The Department of Defense announced on 3 December the beginning of a new satellite program called Project Discoverer. It will consist of the launching of a series of 1300-pound satellites, on an average of one a month, to develop: (i) a manned satellite; (ii) an early-warning satellite for the detection of enemy missiles; and (iii) a means for safely returning satellites to the earth for the recovery of occupants, films, instruments, or other "payloads" too valuable to lose. The project will be directed by the Advanced Research Projects Agency.

The first satellite will be launched late this year or early next year from the new Pacific Missile Range on the coast of Southern California. The launching pads are located at the Vandenberg Air Force Base, about 120 miles northwest of Los Angeles.

The satellites in the Discoverer series will be capable of carrying payloads of several hundred pounds and will be launched into polar orbits by directing them in a southerly direction. Orbits that will carry satellites over the North and South Poles are necessary for certain projects. A satellite in a polar orbit will travel over the entire surface of the globe. Actually, its path will remain fixed in space as the earth rotates inside it.

Cape Canaveral in Florida will continue to be used for satellite and space-probe launchings to the east and southeast. Launchings from the Pacific Missile Range will be only toward the south.

### **World Population and Agricultural Productivity**

The world should support a population of 6 billion in the next century. This is the calculation of G. V. Jacks, one of Europe's leading soil experts and director of the Commonwealth Bureau of Soils at Rothamsted Experimental Station, Britain's chief center for agricultural research, in an article included in the most recent annual report of the Smithsonian Institution. However, Jacks emphasizes that his conclusion depends on a proper organization of the burgeoning society. Fertility of the soil must be maintained everywhere, a far more important factor than bringing new land into cultivation.

There is a curious relationship be-

tween distribution of population and agricultural productivity, Jacks points out. By and large, land fertility increases with the size of towns, not with the number of persons engaged in farming. At first, crop land does little more than supply food for the actual cultivators. Little or nothing is left to put back into the land out of which something is taken by each successive crop. Exhaustion comes soon and the people must find new land.

Then a surplus population flocks together to establish towns supported by industries. They require some of the farm products, and this need tends to make agriculture more stationary in the neighborhoods of towns. Actual money flows back to the farmers. They are able to buy fertilizers or apply more effective measures to prevent soil depletion and raise bigger crops. The process is continuous as long as the industrial centers continue to pour more and more back into the land. Jacks continues:

"Will the world of a hundred years hence be able to feed the 6000 million people who will then be in it? The answer is yes, provided most of them live in towns and produce enough wealth to pay for the food they need. If they offer enough money for their food, the food will be produced."

### Coeducation in Turkey

Robert College and the American College for Girls in Istanbul, Turkey, have merged, paving the way for a Western-style coeducational college, effective next September. Two of the oldest American schools in the Near East, the colleges have a combined enrollment of 1800. Robert College this year has 1150 men students, while 650 women attend the College for Girls. Alfred Ogden of New York City was elected chairman of the new board. Duncan S. Ballantine will continue as president.

Although courses were designed primarily for young Turks, students from 50 nations have studied at the two colleges. Robert, founded in 1863, claims to be the first American college established overseas. It is chartered under the Board of Regents of New York State. The American College for Girls was given a charter under Massachusetts law in 1891. The campuses lie less than 3 miles apart on heights overlooking the Bosphorus.

### Homicide in the United States

In contrast to the marked increase in other major crimes, the incidence of homicide in the United States has decreased in the period since World War

II, according to statisticians of the Metropolitan Life Insurance Company. The homicide rate fell about one-fifth between 1946-47 and 1955-56, from 6.1 to 4.8 per 100,000 of population.

The relative decline was greater for white than for nonwhite persons, and for each race was considerably greater for males than for females. Among white males, the decrease amounted to one-fourth; among nonwhite males it was one-fifth.

Among white people, the homicide rates vary but little in the range of ages from early adult life through middle age, and decrease only moderately at the older ages. Among nonwhites, and particularly for males, the toll from homicide rises to a definite peak in the late 20's and early 30's, and then falls rapidly with advance in age.

Despite the marked increase in juvenile delinquency in recent years, the homicide rate at ages 15-19 decreased. Moreover, the rate at these ages is much lower than that for most adult age groups.

### Germ-Free Laboratory

A new and simplified germ-free laboratory, believed to be virus-proof as well, has been successfully tested at the University of Michigan Medical Center. A goal of biological scientists since the turn of the century, the apparatus is an outgrowth of two other systems developed in the United States and Sweden.

Guinea pigs born in the sterile laboratory last September have survived. The achievement recalled stormy debates that raged early this century on the proposition that all animal life depends, for its very existence, on certain "beneficial bacteria" prevalent in normal life. The apparatus is a sealed metal and glass box about the size of a deep-freeze cabinet. It was designed by Richard Horton, a former postgraduate student at Michigan who is now with the National Institutes of Health.

Nothing rots inside the miniature laboratory. Excess food and animal feces have remained for weeks without decomposing and without odor. Guinea pigs were delivered by Caesarean section directly into the cabinet, employing an intricate surgical procedure that used a plastic membrane to prevent possible contamination by the mother's body. By means of sealed-in rubber gauntlets, investigators can work in the sterile area.

A pressure compartment attached to one end of the unit permits steam sterilization of food and equipment. All air entering the cabinet is first heated to temperatures above 750°F and then cooled. These precautions kill all living

organisms, and have prevented contamination for more than 4 months. It is believed, though not tested, that the apparatus will prove as invulnerable to environmental viruses as it is to germs.

### News Briefs

The AAAS has received a \$250,000 grant from the Carnegie Corporation of New York to continue until 1961 its nationwide program to improve the teaching of science and mathematics in the secondary schools. The Science Teaching Improvement Program is headed by John R. Mayor, director of education for the AAAS. For details of the program's first years—it was launched in 1955 with Carnegie support—see the article on page 1262 of the 21 November issue of *Science*.

\* \* \*

Dedication exercises were held on 5 December for the U.S. Department of Agriculture's new National Seed Laboratory, just completed at Colorado State University at Fort Collins. The laboratory will provide storage for seeds of thousands of different plants—representing the world's most valuable food, feed, pasture, fiber, and tree crops—for use as breeding stock. The Crops Research Division of USDA's Agricultural Research Service will administer the new facility. Operations will be supervised by Edwin James, director of the laboratory and Louis N. Bass, seed physiologist.

\* \* \*

The Woods Hole Oceanographic Institution reports that its new 214-foot research vessel *Chain*, the fourth ship in the institution's ocean-going fleet, left on 6 December for a 16-day cruise between Nova Scotia and Bermuda. The *Chain*, equipped with four large laboratories, has accommodations for a crew of 33 and 28 scientists. She has a cruising range of 10,500 miles. On 2 January she will begin a 3½-month trip for the International Geophysical Year in the southern South Atlantic, and on 1 May she will depart for a 3-month cruise to study the bottom of the Mediterranean.

\* \* \*

Two vocational guidance booklets on careers in chemical engineering and chemistry have recently been published by the Chemical Institute of Canada. The booklets discuss job opportunities, salaries, and the two professions in general. For free copies, write to the institute at 18 Rideau Street, Ottawa 2, Ontario.

\* \* \*

The Medical Research Center at Brookhaven National Laboratory was dedicated on 16 December, following a 2-day conclave of deans of medical colleges. The dedicatory address was de-



livered by Shields Warren, pathologist at New England Deaconess Hospital and professor of pathology, Harvard Medical School. John A. McCone, chairman of the Atomic Energy Commission, also spoke at the ceremonies. The \$6,500,000 center includes a tank-type reactor, a 48-bed hospital for research patients, and laboratories for studies in biochemistry, medical physics, microbiology, pathology, and physiology. The reactor is the first in this country to be designed specifically for medical research purposes.

\* \* \*

The Soviet Union has converted one of its submarines into a scientific laboratory and is sending the vessel on its first prolonged mission this month. An article in *Pravda*, which did not provide an itinerary, said that the submarine will be in the service of the Research Institute of Marine Fishing and Oceanography. The report announced that the vessel would collect data in the seas and oceans and would gather information on new fishing districts.

\* \* \*

Approximately 18,000 high school and college teachers of science and mathematics will benefit during the summer of 1959 from teacher training programs sponsored by the National Science Foundation at 350 institutes in 255 educational institutions. Some \$21 million has been awarded for the support of the summer institutes, which will be held in all 49 states, Hawaii, Puerto Rico, and the District of Columbia. Roughly 300 of the institutes will be open only to high school teachers. Approximately 30 will be for college teachers only, and about 20 will be for both high school and college teachers. Sixteen thousand high school teachers and 2000 college teachers will participate.

\* \* \*

Telev viewers will see the first rocket observations of a solar eclipse and the first above-the-atmosphere views of the sun's activity during an eclipse, when "High Adventure with Lowell Thomas" is broadcast on 10 January, 10 to 11 P.M. (E.S.T.) on the CBS Television Network. The television film was recorded by Thomas and two cameramen from the decks of the U.S.S. *Point Defiant* off the coast of Puka-Puka, an atoll in the Cook Island group in the South Pacific Ocean. The expedition was conducted by the Naval Research Laboratory.

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Herbert Kubitschek of Argonne National Laboratory has modified a commercial electronic cell counter so that it can be used for the counting and sizing of bacteria as individuals. This has opened the way for the counter's use in geological, meteorological, and agricultural studies.

## Scientists in the News

RENATO DULBECCO, professor of biology at California Institute of Technology, has been named by the Board of Directors of City Trusts of Philadelphia, Pa., to receive the John Scott Award for his development of a method for demonstrating the presence of viruses in tissues. His method provided a technique for the production of plaques with animal cells. This technique permits an accurate determination of the activity of animal viruses and has played an important part in the effort to combat virus diseases. Salk and others have used this method, or modifications of it, in the preparation of vaccines. The award will be presented at the zoologists' dinner meeting that is to be held on 29 December in Washington, D.C., as a part of the AAAS annual meetings.

The John Scott Award was established by an obscure Scotch chemist of the same name, who resided in Edinburgh until his death in 1816. He bequeathed \$4000 to the city of Philadelphia, the income of which was to be "laid out in premiums to be distributed among ingenious men and women who make useful inventions. . . ." By 1917, the fund had grown to \$100,000. This year, awards of \$2000 may be made, but the standard award has been set at \$1000.

PAUL GYORGY, professor of pediatrics at the University of Pennsylvania and chief of the Pediatric Service of the Philadelphia General Hospital, is to receive the degree of honorary medical doctor from the University of Heidelberg, Germany, of which he is an alumnus and former faculty member. The degree is conferred rarely, usually in recognition of a particularly outstanding achievement in the field of medicine. Gyorgy is being honored for his many scientific achievements, which include the discovery of riboflavin.

Another recipient of the special degree will be OTTO WARBURG of Berlin, Germany, a Nobel laureate and developer of the Warburg apparatus, which is used in research laboratories all over the world.

Major General JOHN B. MEDARIS, commanding general, U.S. Army Ordnance Missile Command, received the Michael I. Pupin Anniversary Medal of the Columbia Engineering School Alumni Association on 2 December for "distinguished service to the nation."

MAURICE ROY, director, Office National d'Etudes et de Recherches Aeronautiques, accepted the invitation of the Institute of the Aeronautical Sciences to deliver the 22nd Wright Broth-

ers Lecture on 17 December, 55th anniversary of the Wright's famous flight. The lecture, "Means and Examples of Aeronautical Research in France," was heard at the Smithsonian Institution, Washington, D.C. It will be repeated at IAS section meetings in Cleveland, Ohio, on 18 December; Dallas, Tex., on 19 December; and Los Angeles, Calif., on 22 December.

ALEXANDER H. LEIGHTON, professor of psychiatry at Cornell University, delivered this year's Thomas William Salmon lectures at the New York Academy of Medicine. His subject was "An Introduction to Social Psychiatry," which he discussed in an afternoon and evening lecture on 4 December.

In celebrating its 100th anniversary this year, E. R. Squibb & Sons is sponsoring visiting lectureships in the United States by foreign scientists, all well-known specialists in particular disciplines. Outstanding American scientists are also included in the program. Virtually every medical school in the country has arranged to have one of the lecturers appear before faculty and student groups sometime during the 1958-59 academic year.

Lecturers from abroad who have already completed their tours are as follows: MACDONALD CRITCHLEY of the National Hospital, London, England, "The Study of Language Disorders Past, Present and Future"; and LUIS F. LELOIR of the Biochemistry Research Institute, Buenos Aires, Argentina, "The Role of Uridine Nucleotides in Metabolism."

In February and March, JOHN C. ECCLES of the John Curtin School of Medical Research, Australian National University, Canberra, will discuss "Problems of Organization and Plasticity at the Simplest Levels of the Mammalian Nervous System"; JAMES DANIELLI, professor of zoology at King's College, University of London, London, England, will discuss "Designing of Drugs for the Chemotherapy of Cancer"; FEODOR LYNEN of the Max Planck Institute for Cell Chemistry, Munich, Germany, will discuss "The Function of Coenzyme A in Fat and Lipid Metabolism"; and ANDRE M. LWOFF of the Institute Pasteur, Paris, France, will discuss "Factors Influencing the Evolution of Viral Diseases at the Cellular Level and in the Organism."

In April and May, JOHN H. GAD-DUM of Edinburgh University, Edinburgh, Scotland, will speak on "The Pharmacological Analysis of Tissue Extracts," and JOHN F. BROCK of the University of Cape Town, Wirmher & Beit Medical Laboratories, Observatory Cape, Union of South Africa, will speak



on "Human Nutrition and Its Growing Importance to Clinical and Investigational Medicine." For detailed schedules, write to Squibb at 745 Fifth Ave., New York.

GUSTAVE FREEMAN, former head of the clinical pharmacology and therapeutics section of the Cancer Chemotherapy National Service Center, Bethesda, Md., has joined the biological sciences department at Stanford Research Institute, Menlo Park, Calif., as program director of medical research. He will direct preclinical cancer research at S.R.I. and clinical studies conducted with neighboring hospitals. Concurrently, he will carry out research on nucleic acids with G. W. Beadle at California Institute of Technology. The two men will study the action of selected cancer chemotherapeutic agents on nucleic acids.

FREDERICK P. THIEME, assistant to the president at the University of Washington, has been named provost of the university. Thieme was chairman of the department of anthropology at the University of Michigan before joining the University of Washington on 1 August.

The following mathematicians have reported new appointments for the academic year 1958-59.

G. W. MORGENTHAU of the Institute for Air Weapons Research, University of Chicago, has been appointed associate professor in the undergraduate division of the University of Illinois, Chicago.

KATSUMI NOMIZU, assistant professor at Nagoya University, Japan, has been appointed associate professor at the Catholic University of America.

ALEXANDER ORDEN of the Burroughs Corporation has been appointed a professor in the School of Business, University of Chicago.

M. M. PEIXOTO, professor on leave from the University of Brazil, has accepted a position as staff scientist with RIAS, Inc., Martin Company, Baltimore, Md.

H. W. REDDICK, professor emeritus of New York University, has been appointed visiting professor at Syracuse University.

R. F. RINEHART, professor on leave from Case Institute of Technology, will be director of special research and operations research at Duke University.

LOUISE J. ROSENBAUM, associate professor on leave from Saint Joseph College, Connecticut, will be in Oxford, England.

R. A. ROSENBAUM, professor on leave from Wesleyan University, has been awarded a National Science Founda-

tion science faculty fellowship and will be at Oxford University, England.

S. A. ROWLAND, professor emeritus of Ohio Wesleyan University, has been appointed a lecturer at Ohio State University.

S. M. SHAH, professor of Muslim University Aligarh, India, has been appointed visiting professor at the University of Wisconsin, Madison.

JOHN D. SPIKES is on a 2-year leave from his regular position as professor and head of the department of experimental biology at the University of Utah. He is serving as a specialist in cell physiology with the U.S. Atomic Energy Commission's Division of Biology and Medicine, Germantown, Md.

DAVID A. RYTAND has been named the first Bloomfield professor of medicine at the Stanford University Medical School. The professorship honors ARTHUR L. BLOOMFIELD, emeritus professor of medicine who retired in 1954. Bloomfield is now primarily engaged in adding to his already extensive writings on internal medicine.

Rytand, a native San Franciscan who earned both the A.B. and M.D. degrees at Stanford, became a member of the medical faculty in 1936. He is editor of the *Annual Review of Medicine*, a member of the editorial board of the *Journal of Chronic Diseases*, and the author of many scientific papers on heart and kidney diseases.

LESLIE H. MEREDITH has been appointed head of the Rocket Sonde Branch, U.S. Naval Research Laboratory, Washington, D.C. He has been with the laboratory since 1954.

T. B. MASSALSKI, Polish-born scientist who is a solid state physicist, has been appointed senior fellow in the metal physics fundamental research group at the Mellon Institute, Pittsburgh, Pa., effective 1 January. He obtained his Ph.D. from the University of Birmingham, Birmingham, England, where he is now a lecturer in physical metallurgy. He has been a postdoctoral fellow at the Institute of Metals, University of Chicago; consultant to the Max Planck Institute for Metals Research, Stuttgart, Germany; and consultant and lecturer at Battelle Memorial Institute, Columbus, Ohio.

DONALD A. HARRINGTON, associate professor of speech at the University of Florida, has been appointed to the newly created post of specialist in speech and hearing in the U.S. Office of Education, effective 1 February. He will be concerned with school programs for children and youth with impaired speech

and hearing. He will be a member of the Section on Exceptional Children and Youth, which is headed by Romaine Mackie.

JERRE L. NOLAND, chief biochemist, Research Laboratory, Veterans Administration Center, Wood, Wis., has accepted an appointment as chief, Medical Research Laboratory, Veterans Administration Hospital, Louisville, Ky. He will also be a research associate (associate professor) in the department of biochemistry of the University of Louisville School of Medicine.

LEON SVIRSKY has been appointed science editor of Basic Books, New York publishing house. For 11 years, until his resignation this fall, Svirsky had been managing editor of *Scientific American*.

## Recent Deaths

BERTRAM M. BERNHEIM, Baltimore, Md.; 78; associate professor emeritus of surgery at Johns Hopkins Medical School; founder of the American College of Surgeons; wrote *Blood Transfusion, Hemorrhage, and the Anemias* in 1917, when transfusion work had just started; 28 Nov.

HIGDON B. ELKINS, Iowa City, Iowa; 51; professor of radiology at the State University of Iowa's College of Medicine; 29 Nov.

WILLIAM J. FARRISEE, Hoboken, N.J.; 60; professor of engineering and dean of men at Stevens Institute of Technology; dean of men at Clarkson College of Technology, Potsdam, N.Y., 1946-55; had been connected with Clarkson for 50 years; 1 Dec.

ROBERT S. JANE, Montreal, Canada; 59; plant chemist and president of Shawinigan Chemicals Ltd.; president of the Chemical Institute of Canada, 1952-53; chairman of the Canadian section of the Society of Chemical Industry in 1957; 2 Dec.

CHARLES A. MAGOON, Mesa, Arizona; 75; retired food technologist, U.S. Department of Agriculture; 8 Nov.

LEILA T. NEWCOMB, Albany, N.Y.; 88; before retirement in 1952, a social worker at Hartley House in New York for 40 years; 2 Dec.

Sir HUBERT WILKINS, Framingham, Mass.; 70; well-known polar explorer and geographer; consultant to the Army Quartermaster Corps Research and Development Center in Natick, Mass.; completed the first flight over the polar regions from North America to Europe in 1926, for which he was knighted by King George V of England in 1928; tried to open an Arctic submarine route by passing under the polar ice cap in 1931; 1 Dec.

## Book Reviews

**Isaac Newton's Papers and Letters on Natural Philosophy and Related Documents.** I. Bernard Cohen, Ed., assisted by Robert E. Schofield. Harvard University Press, Cambridge, 1958. xiii + 501 pp. Illus. \$12.50.

One of the great intellectual phenomena of the present age is the increasing interest in the writings of Isaac Newton. The cause of this increased interest may be ascribed to two fundamental factors, namely (i) the rapid development of physical sciences and (ii) the demand for the historical antecedent for our present state of scientific progress.

The editor, I. B. Cohen, has done a great service to this intellectual growth of Newtonianism in producing an excellent source book for the layman and, more particularly, for the student of physical sciences, as well as for the historical scholar in science, who at this moment is on the increase, especially in the United States. Because of the many ramifications of Newton's writings and thoughts, this book should have a wide appeal. The preface and introduction are of a general nature in describing the papers and paying tribute to the contributing scholars for their work. Particular notice is given to the Bundy Library and its director, Bern Dibner, who has made publication of this work possible.

The book opens with Newton's 15 papers on physical optics. These papers are reproduced as they were published in the *Transactions of the Royal Society of London* during the period from 1671 to 1676, with a good historical introduction by T. S. Kuhn of the University of California. The paper on *Chemical Philosophy*, with an introduction by Marie Boas, indicates that Newton was more modern in his thoughts than has been recognized. Dr. Boas calls attention to a famous paper of Newton's which really marks him as a chemist of the Robert Boyle type. This rare paper, "Some thoughts about the nature of acids" (*Lexicon Technicum* 2 vols., 1710) is in the Stanford-Newton collection and its reproduction here is indeed appropriate.

For those who wish to know of the transcendental mind of Newton and his philosophy of nature, Perry Miller of

Harvard University gives an excellent introduction to the four famous letters from Newton to Richard Bentley and to the Boyle lectures, *Confutation of Atheism*. The final paper on "Fontenelle and Newton" is probably the first authentic biography of Newton. It has an interesting introduction by Charles C. Gillespie of Princeton University. *Halley and The Principia*, with an introduction by Robert E. Schofield of the University of Kansas, was the first book review of Newton's great work.

The appendix, namely the comments on Birch's *History of the Royal Society*, brings to the public's attention further comments upon the papers printed in this volume and should not be overlooked by any student of Newton. The extensive footnotes in all six chapters are important to the continuation of sources for Newton's biography and papers.

The book is well printed, and the photographic reproductions are clear and sharp. Much more could be said of this valuable contribution to Newtonian literature, but space forbids. The beautiful portrait of Newton is reproduced from an original painting by E. Seeman, painted in 1726, and is probably the most authentic picture of Newton in his prime.

FREDERICK E. BRASCH

Stanford University

### Processed Plant Protein Foodstuffs.

Aaron M. Altschul, Ed. Academic Press, New York, 1958. xv + 955 pp. Illus. \$26.

This book is much more comprehensive than its title indicates and addresses itself to a far greater circle of scientifically and professionally interested people than those concerned with the manufacture and use of processed plant proteins. In a time of expanding world population and increasing demand for more and better foods and feedstuffs, attention of agronomists, nutritionists, plant breeders, husbandmen, demographers, and technologists is focused on the two-sided problem of how to provide mankind economically with a maximum of animal

products by using scientifically grown forage and feedstuffs as well as farm and factory waste products to feed ruminating and nonruminating animals and how to provide an abundance of nutritionally adequate vegetable proteins for the large section of mankind which, for economic or religious reasons, consumes no animal products.

Any other author would have shrunk from the immensely difficult task of answering these crucial questions in one volume, but not Altschul, the scholarly and yet practical-minded principal chemist of the Department of Agriculture's Seed Protein Pioneering Research Laboratory in New Orleans. He realized the great need for such a book, especially in overpopulated and underdeveloped areas of the world where more and more emphasis is being placed on a qualitatively and quantitatively adequate vegetable diet, but he also realized that such a tremendous task requires the combined efforts of competent specialists in the field of animal and human nutrition, botany, biochemistry, microbiology, and food technology. He was successful in bringing together a group of eminent scientists and technologists, and while leaving each contributor utmost freedom to deal with those aspects of the subject matter with which he was most familiar, he himself provided such unity and consistency of treatment that one gets the impression that he is reading a book by a single author.

After a short survey of protein nutrition and plant proteins in general the book deals, in the first section, with the properties of processed plant proteins which affect use of these proteins as animal or human food. Since the great bulk of plant proteins are the meals or cakes of oilseeds, these are given the most exhaustive treatment. Here the chapters "Use of processed plant proteins as human food," by R. F. Dean of Kampala, Uganda, and "Vegetable protein isolates," by M. L. Anson of Cambridge, Mass., make fascinating reading indeed as they afford glimpses into the future in the field of nutrition. "Given Nature's supply of a cheap plant protein of high nutritional value" states Anson, "the technologist and the factory can do many of the manufacturing jobs that have been done, at high costs, only by animals."

The second part of the book deals with the processing of individual plant proteins and is remarkable in its comprehensiveness; it covers not only the numerous oilseeds but also alfalfa and other leaf meals, peas and beans, fermentation and milling by-products, and microbial and algal proteins. In a most interesting chapter—"Cottonseed meal"—Altschul and his co-workers show that the protein of cottonseed is of relatively high nutrient

value and could be made available for nutrition of nonruminants and human beings by removal or inactivation of toxic gossypol.

In my opinion the book is a "must" for every scientific and technical library and will serve for a good many years as a competent guide in an extremely important and rapidly progressing field in which scientists and technologists, agriculturists and industrialists, and economists and nutritionists work hand in hand for the welfare of mankind.

FRANCIS JOSEPH WEISS  
Arlington, Virginia

#### Guide to Russian Medical Literature.

Scott Adams and Frank B. Rogers, Eds. National Library of Medicine, Washington, D.C., 1958 (order from Superintendent of Documents, U.S. Government Printing Office, Washington 25, D.C.). iv + 90 pp. \$0.40.

The ascent of Sputnik in the fall of 1957 gave rise to a sudden realization that we knew little more about Soviet science than we did about what goes on in the minds of the leaders of the Soviet Union. However, in scientific circles at least, this awareness predated Sputnik by a number of years. As far back as 1949 or 1950, the British Department of Scientific and Industrial Research had begun issuing its *Translated Contents List of Russian Periodicals* to meet a need created by a 1947 policy change under which scientific publications emanating from the Soviet Union appeared in the Russian language only; the American Mathematical Society had undertaken, around the same time, a series of translations of basic Russian papers in mathematics, and various other groups in this country had begun publishing cover-to-cover translations of Soviet journals in physics and chemistry.

Medicine was a rather late entry in the Russian translation field. Major activity in translating in the field of medicine did not begin until 1956, when the U.S. Senate Appropriations Committee made available funds to the National Institutes of Health for the organization of a Soviet information program. *Guide to Russian Medical Literature* is an outgrowth of this program.

There is an obvious need for guides to Soviet scientific literature among scholars and librarians, and *Guide to Russian Medical Literature* serves very nicely in its field, covering both Western-language and Russian-language sources of Soviet medical information, sources of translation, and methods of procurement of Russian medical publications and listing basic Soviet books and journals in the field. The book is keyed to the practical

question of "how to get it" and does a good job of providing the answer.

There is a hint of special pleading in some of the passages having to do with present translation programs in the United States, and one could argue with some of the points raised to justify these programs. However, neither the justifications nor any arguments against them seem necessary. Any effort to expand the availability of a relatively inaccessible body of knowledge is bound to be a step in the right direction.

There are two rather unfortunate chapters at the end of the book which are translations of Russian articles on the development of Russian medical libraries and Russian medical publishing. Both chapters exhibit the Soviet preoccupation with numbers and the Soviet willingness to stretch the truth and twist it a little in order to make a point. These two chapters mix a good deal of misguidance with the guidance they offer. The book would not have suffered and probably would have benefited from their omission.

SAUL HERNER

Herner and Company,  
Washington, D.C.

#### Quantum Mechanics of One- and Two-

Electron Atoms. Hans A. Bethe and Edwin E. Salpeter. Springer, Berlin; Academic Press, New York, 1957. viii + 369 pp. Illus. \$10.

It has been said that when a physics book first appears one cannot trust its equations and that by the time it has been reprinted the text is out-of-date. The present volume—an exact reproduction, with the omission of Dumond and Cohen's article, of volume 35 of the *Encyclopedia of Physics*, edited by S. Flügge—steers a happy course between these two accusations.

First of all, while the *Encyclopedia* article itself is partially based upon Bethe's article of the same title in the Geiger and Scheel *Handbuch* of 1933, the text of the joint Bethe-Salpeter work has very definitely been brought up-to-date. Second, the present book (which sells at 2.7 cents per page) includes nine pages of addenda and errata (mainly updating the *Encyclopedia* article to mid-1957), a preface, and two indexes, in addition to the article from the *Encyclopedia* (which sells at 5.3 cents per page).

The aim of this book is twofold. First, as a reference work, it summarizes the calculations that have been performed on hydrogen-like and helium-like atoms and compares them with results obtained by experiment. Second, it is also a practical text for the study of applied quantum mechanics, especially in view of the vast

array of generally useful mathematical tricks and approximation techniques which are included. Only the elements of quantum theory are presupposed.

The authors begin with a nonrelativistic treatment of the free hydrogen atom, including a detailed solution (in 23 pages) of the relevant Schrödinger equation in spherical coordinates. There follow sections on the Dirac theory and on radiative and other relativistic corrections for the free hydrogen atom. In the next part, the free helium atom is handled both nonrelativistically and relativistically. In part 3 the influence of external fields is described in sections on the Zeeman effect and the Stark effect. The final part considers interactions with radiation—the discrete spectrum, the photoeffect, and bremsstrahlung.

The book is definitely pedestrian when it comes to field theory. No formal derivations of quantum electrodynamics are given, but specific application to atomic systems of general field-theoretic results is described in detail.

Despite its pedigree, this volume contains some typographical errors. I noted about five such errors, all of them obvious. For example, note 3 on page 354 should read 0.124 and 0.160 rather than 1.24 and 1.60.

Nevertheless, this book is and will remain the standard treatment of the one- and two-electron atoms. It is an orderly, integrated summary of all that has been done, rendered in the simplest way compatible with the calculations.

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**The Sloane Herbarium.** An annotated list of the *Horti Sicci* composing it; with biographical accounts of the principal contributors. Based on records compiled by the late James Britten, with an introduction by Spencer Savage. Revised and edited by J. E. Dandy. British Museum (Natural History), London, 1958. 246 pp. Illus. + plates. £7 7s.

The remarkable herbarium assembled by Hans Sloane during the latter part of the 17th and first part of the 18th centuries (now preserved in the department of botany of the British Museum of Natural History) contains numerous valuable type specimens and is a virtual "mine" of botanical and horticultural historical information. That the abundance of source material present in this collection has not been appreciated or adequately drawn upon by those concerned with the natural history of the period has been amply demonstrated by the authors of the volume under review.



The Sloane Herbarium consists of 265 volumes comprising 337 numbered *Horti Sicci*. Sloane himself collected mainly in Jamaica, Barbados, Nevis, and St. Kitts, and these specimens were an important basis for published work on the rich flora of the West Indies. But most of the specimens were collected by Sloane's contemporaries. The largest of these collections were assembled by William Courten, by James Petiver, and by Leonard Plukenet. The Petiver and Plukenet collections contain American plants which, through published illustrations, became the basis for names supplied by Linnaeus. The collections of Mark Catesby from Carolina, Florida, and the Bahama Islands, as well as that of John Bartram from the area around Philadelphia, are important to American botanical history. Actually, many of the *Horti Sicci* of Sloane do contain American plants. For example, *H.S. 74* comprises "plants gathered in Maryland by Mr. Jones a minister, Dr. Krieg, and Mr. Vernon, and by them given to Mr. Ayrie."

It is important to keep in mind that Dandy's book, *The Sloane Herbarium*, attempts to give the reader an insight into what is contained in the Sloane collections, but is not a major source book in itself, even though there are many hints and suggestions for the discerning researcher.

REED C. ROLLINS

Gray Herbarium of Harvard University

**Progress in Organic Chemistry.** vol. 4. J. W. Cook, Ed. Academic Press, New York; Butterworth, London, 1958. ix + 256 pp. Illus. \$8.80.

Volume 4 of this series includes the following chapters: (i) "Naturally occurring unsaturated fatty acids" (25 pages, 151 references), by F. D. Gunstone; (ii) "Free valence in conjugated organic molecules" (36 pages, 155 references), by B. Pullman and A. Pullman; (iii) "Oxygen heterocyclic fungal metabolites" (40 pages, 72 references), by U. B. Whalley; (iv) "Naturally occurring 2-acylcyclohexane-1,3-diones" (22 pages, 80 references), by C. H. Hassall; (v) "Degradation and synthesis of peptides" (65 pages, 484 references), by A. H. Cook and G. Harris; and (vi) "Heterocyclic derivatives of phosphorus, arsenic and antimony" (29 pages, 65 references). There is a 7-page index.

Among the fatty acids discussed in chapter 1, the most striking ones are perhaps those which appear to contain a cyclopropene ring. The author agrees with the  $\omega$ -(2-n-octylcycloprop-1-enyl) octanoic acid structure for stercularic acid. It is commendable to have in a book of this type a chapter on free valence ("a measure of the residual unutilized bond-

ing possibilities of carbon atoms"). The treatment is clear enough, since the mathematical developments have all been left in the original references. A correlation between free valence and localization energy is undoubtedly attractive to the organic chemist, who would like nothing better than a neat map of reactivity with each structural formula.

Chapter 2 discusses this information, which, however, will have to be accepted ex cathedra. Correlations between free valence and a number of properties, such as resonance energies, acidic and basic strength, dipole moments, and spectroscopic effects, are also given.

Chapter 3 includes the methylene quinones (citrinin and two others), the chromenopyrones (cytomyecetin and five others), the spirocoumarin-3-ones (griessfulvin and two others), and the depsidones. Reference is made to the acetate hypothesis of biogenesis and to the formate and propionate variations. Chapter 4 contains very interesting chemistry, including the usnic acid problem, with an all-too-brief exposition of Barton's elegant synthetic solution.

Chapter 5 will become, probably, one of the best points of departure for gaining an acquaintance with peptide chemistry. Chapter 6 is essentially a compilation of work by F. G. Mann and his coworkers. It may not be superfluous to point out that the "heterocyclic derivatives" of the title are all of the saturated type. The reader should not expect to find anything on the aromaticity of group V heterocycles.

This is a worthy addition to the series of valuable reviews appearing under the editorship of J. W. Cook.

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## New Books

*Amid Masters of Twentieth Century Medicine.* A panorama of persons and pictures. Leonard G. Rowntree. Thomas, Springfield, Ill., 1958. 702 pp. \$11.50.

*Anatomie de latimeria chalumnae.* vol. 1, *Squelette, muscles et formations de soutien.* J. Millot and J. Anthony. Publie avec le concours de l'Institut de Recherche Scientifique de Madagascar, Tananarive, par les Editions du Centre National de la Recherche Scientifique, Paris, 1958. Text, 122 pp.; plates, 80 pp. 1958 Annual International Conference on High Energy Physics at CERN. *Proceedings.* Sponsored by the International Union of Pure and Applied Physics, Geneva, 30 June-5 July 1958. B. Ferretti, Ed. European Organization for Nuclear Research, Geneva, 1958. 356 pp. F. 45.

*Antibiotics.* Their production, utilization and mode of action. A symposium held at the Hindustan Antibiotics (Private) Ltd., Pimpri, 27-30 March 1956. Council of Scientific & Industrial Re-

search, New Delhi, 1958. 317 pp. Rs. 15.

*The Archeology of Coastal North Carolina.* William G. Haag. Louisiana State Univ. Press, Baton Rouge, 1958. 147 pp.

*Atomic Terminology.* English, German, French, Italian. Lore Lettenmeyer. Isar Verlag, Munich, Germany, 1958. 298 pp. The purpose of this dictionary is to provide the essential scientific and technical terms used in atomic and nuclear physics, reactor engineering, radiation physics, and associated fields, with the object of facilitating the study of the relevant foreign literature on the subject. The main section of the dictionary is based on English. The terms are listed alphabetically and numbered consecutively. German, French, and Italian equivalents are given in parallel columns with the same numbers. This section is followed by alphabetically arranged German, French, and Italian indexes listing the terms with the numbers under which the corresponding terms in the other languages will be found in the main section.

*Big Molecules.* Harry Melville. Macmillan, New York, 1958. 180 pp. \$3.95.

*Biochemical Preparations.* vol. 6. Carl S. Vestling, Ed. Wiley, New York; Chapman & Hall, London, 1958. 114 pp. \$5.25.

*The Chemical Behavior of Zirconium.* Warren B. Blumenthal. Van Nostrand, Princeton, N.J., 1958. 404 pp. \$11.

*The Chemical Kinetics of Enzyme Action.* Keith J. Laidler. Oxford Univ. Press, New York, 1958. 426 pp. \$9.60.

*Contemporary Sociology.* Joseph S. Roucek, Ed. Philosophical Library, New York, 1958. 1221 pp. \$12.

*Deficiency Disease.* Fundamental and structural changes in mammalia which result from exogenous or endogenous lack of one or more essential nutrients. Richard H. Follis, Jr. Thomas, Springfield, Ill., 1958. 590 pp. \$14.75.

*Directory, American Council of Independent Laboratories.* A guide to the leading independent testing, research, and inspection laboratories of America. American Council of Independent Laboratories, ed. 7, 1958 (order from Harold M. Dudley, Executive Secretary, 4302 East-West Highway, Washington 14). 100 pp.

*Effect of Surface on the Behaviour of Metals.* Lectures delivered at the Institution of Metallurgists Refresher Course, 1957. Iliffe, London; Philosophical Library, New York, 1958. 107 pp. \$10.

*Electronics of Microwave Tubes.* W. J. Kleen. Translated by P. A. Lindsay, A. Reddish, C. R. Russell. Academic Press, New York, 1958. 370 pp. \$9.

*Elementary Seismology.* Charles F. Richter. Freeman, San Francisco, 1958. 776 pp. \$12.

*Elements of Biophysics.* James E. Randall. Year Book, Chicago, 1958. 333 pp.

*Essential Fatty Acids.* Fourth International Conference on Biochemical Problems of Lipids, Oxford, 15-18 July 1957. H. M. Sinclair, Ed. Academic Press, New York; Butterworths, London, 1958. 286 pp. \$9.50. The papers were organized in the following divisions: Chemical aspects; Adsorption and distribution; Biochemical functions; General discussion of essential fatty acids. An author index, a subject index, and a list of participants is included.



# Reports

## Inherited Electrophoretic Hemoglobin Patterns among 20 Inbred Strains of Mice

**Abstract.** The hemoglobin from mice of six inbred strains is of the single-spot electrophoretic type, and that from 14 inbred strains is of the diffuse type. No selective advantage is apparent for either type. The distribution among strains shows some relation to the history of the development of the strains.

Recent studies by Ranney and Waelsch (1) have demonstrated two distinct types of hemoglobin in normal healthy mice from four standard inbred strains and from seven special mutant strains. They have also shown that the difference between animals with single-type hemoglobin, giving a single homogeneous spot on filter-paper electrophoresis, and those with diffuse-type hemoglobin is due to a single genic substitution (2, 2a). In the present investigation, the hemoglobin patterns of 8 to 10 mice from each of 20 different inbred strains were determined by one of us (P.S.G.) by means of a modification (3) of the starch block electrophoretic technique developed by Kunkel *et al.* (4). The mice were young adults (6 to 9 weeks old) of both sexes, from the Inbred Nucleus of the Jackson Laboratory. All of the mice tested from any one inbred strain showed the same hemoglobin type (5).

Mice from six inbred strains (C57BL/6, C57BR/cd, C57L/He, C58, SWR, and WK) carried single-type hemoglobin, and mice from 14 inbred strains (A/He, A/Jax, AKR, BALB/c, C3H/Jax, C3HeB, DBA/1, DBA/2, MA/My, RFM, 129, WB, WC, and WH) carried diffuse-type hemoglobin (2a).

**Instructions for preparing reports.** Begin the report with an abstract of from 45 to 55 words. The abstract should not repeat phrases employed in the title. It should work with the title to give the reader a summary of the results presented in the report proper. (Since this requirement has only recently gone into effect, not all reports that are now being published as yet observe it.)

Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to one 2-column figure (that is, a figure whose width equals two columns of text) or to one 2-column table or to two 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to Contributors" [Science 125, 16 (1957)].

The mean erythrocyte number and size characterizing young adults of ten of these inbred strains has been established by previous investigations (6). Three single-type strains (C57BL/6, C57BR/cd, and C57L/He) gave mean erythrocyte values of  $9.66$  to  $10.54 \times 10^6$  cells per cubic millimeter, while seven diffuse-type strains (A/He, A/Jax, AKR, BALB/c, C3H/Jax, DBA/1, and DBA/2) gave mean erythrocyte values of  $8.79$ – $10.52 \times 10^6$  cells per cubic millimeter. The mean cell volumes of the single-type strains ranged from  $45.5$  to  $51.1 \mu\text{m}^3$ ; those of the diffuse-type strains, from  $41.4$  to  $48.5 \mu\text{m}^3$ . Thus neither hemoglobin type is associated closely with any particular level of blood-cell values. Data are also available on the life-span of mice from 11 of these inbred strains (7). Mice of all three C57 strains, with single-type hemoglobin, have relatively long life-spans (means for breeding females and males range from 457 to 576 days), but this range is not markedly above that for BALB/c breeders, (mean, 470 days), nor for strain 129 breeders (mean, 556 days), both of which carry diffuse-type hemoglobin. Thus both electrophoretic types of hemoglobin must be regarded as "normal" for mice, with no evidence from blood picture or life-span of selective advantage for either homozygous genotype.

The distribution of hemoglobin type among these inbred strains has an interesting relationship to the history of their development. Figure 1, extended (8) and modified from a previous chart prepared by Heston (9), summarizes the known history and interrelations of the 20 tested inbred strains, indicating the laboratory stock from which each was derived and the approximate time at which brother-sister inbreeding began. Assuming that no mutations occurred during the course of inbreeding, the alleles now fixed in these strains must have been carried in the original noninbred populations from which they have descended. Of course, these stocks need not have been homozygous for the allele ultimately fixed, nor need the allele even have predominated in the noninbred stock. Five of the single-type inbred strains are descended from a single litter in C. C. Little's colony, derived from the well-known Lathrop-Loeb colony (9). Two females, C57 and C58, were mated

to their brother, C52. The recently developed WK inbred strain (10) is derived from a cross between a C57BL female and a noninbred male heterozygous for *Ww*. Existence of the *Hb<sup>1</sup>* allele in the littermate females, C57 and C58, or in their brother, C52, would be sufficient to explain the presence of that same gene in these five inbred strains. It is highly improbable that mice of the sixth inbred strain with single-type hemoglobin, SWR, have any ancestry in common with the C57-58 group. The SWR strain was developed by Clara Lynch at the Rockefeller Institute from mice received directly from deCoulon in Switzerland.

There is some common ancestry known for inbred strains characterized by diffuse-type hemoglobin, as is shown in Fig. 1 and in Heston's analysis (9). However, the 14 inbred strains with diffuse-type hemoglobin are descended from several different noninbred laboratory mouse colonies (2a). The earliest of these noninbred colonies were almost certainly derived independently from the wild or widely separated parts of the Fancy (Little's color stocks and the Ohio dealer's stocks). Furth's A and R stocks may also represent at least one, possibly two, further derivations from the wild. Dunn's color stocks, and the stocks of Waelsch and Holman, may very well have received animals (and consequently hemoglobin-pattern genes) from these early stocks.

The greater frequency of diffuse-type hemoglobin strains suggests wider distribution in nature of the *Hb<sup>2</sup>* allele. However, it may result from greater propagation in the laboratory, for reasons not related to natural selection, rather than

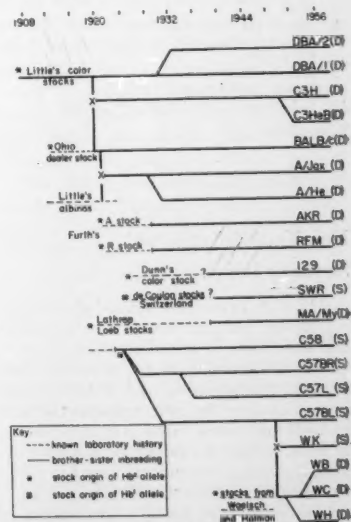


Fig. 1. Known history and interrelations of the 20 inbred strains tested.

from original greater availability. Mice with either type of hemoglobin appear to be normal and healthy, and both alleles must have been present in wild mice to account for the observed strain distribution.

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#### References and Notes

1. H. M. Ranney and S. Glücksohn-Waelsch, *Ann. Human Genet.* 19, 260 (1955); S. Glücksohn-Waelsch, H. M. Ranney, B. Siken, *J. Clin. Invest.* 26, 753 (1957).
2. The symbol for the allele determining single-type hemoglobin is Hb<sup>1</sup>; that for the allele determining diffuse-type hemoglobin is Hb<sup>2</sup> (personal communication from S. Glücksohn-Waelsch).
- 2a. Note added in proof. A new study [J. Rosa, G. Schapira, J. C. Dreyfus, J. deGrouchy, G. Mathé, J. Bernard, *Nature* 182, 947 (1958)], by starch-gel electrophoresis, of hemoglobins from five of the same inbred types of mice as those used in the present work, plus one non-inbred type, suggests that there may be at least four electrophoretically distinct types of mouse hemoglobin. If this proves to be true, then there are probably more than the presently postulated two allelic genes determining hemoglobin type, and their distribution would be expected to show less relationship to strain history than would the distribution of only two.
3. P. S. Gerald and L. K. Diamond, *Blood* 13, 61 (1958).
4. H. G. Kunkel, R. Ceppellini, U. Muller-Eberhard, J. Wolf, *J. Clin. Invest.* 36, 1615 (1957).
5. When these determinations involved Jackson Laboratory sublines of strains tested by Ranney and Waelsch, the results agreed completely. We are indebted to Dr. Ranney for preliminary tests of hemoglobin pattern of mice from inbred strains WB, WC, WH, and WK.
6. E. S. Russell, E. F. Neufeld, C. T. Higgins, *Proc. Soc. Exptl. Biol. Med.* 78, 761 (1952).
7. E. S. Russell, "Information on the Inbred Nucleus Strains, Tumors, and Their Uses" (revised), obtainable from Supply Dept., Jackson Laboratory, on request; A. M. Michelson, E. S. Russell, J. Southard, *Am. J. Physiol.*, in press.
8. Committee on Standardized Nomenclature for Inbred Strains of Mice, *Cancer Research* 12, 602 (1952).
9. W. E. Heston, *Jackson Lab. 20th Anniv. Comm.* (1949), p. 9.
10. E. S. Russell, *Genetics* 41, 658 (1956).

9 June 1958

## New Type Sedative and Soporific Drug

**Abstract.** Trimethoxybenzoyl-glycine-diethylamide induced in dogs and cats normal sleep without preceding ataxia. A five- to ten-fold increase of the soporific dose resulted in restlessness and disorientation instead of sleep. In man, oral doses of 500 to 1500 mg caused sedation or drowsiness, or both, in half the cases. No spindling or drug-induced artifacts were found in electroencephalographic recordings.

Drugs commonly used for hypnotic action in the practice of medicine in human beings are ineffective when similarly ap-

plied in dogs and cats. These species show ataxia accompanied frequently by frank excitement during induction. Similarly, on spontaneous awakening or active arousal, a similar period of disorganized activity results. In the course of an investigation of new compounds with action on the central nervous system, trimethoxybenzoyl-glycine-diethylamide (Riker 548; proposed generic name, trimeglamide) demonstrated the ability to induce in animals a state of somnolence which could not be distinguished from the physiologic state of sleep. This somnifacient action was neither preceded nor followed by the above-mentioned skeletal muscle involvements. No other drug known to us will produce this phenomenon.

In dogs and cats, the oral soporific dose of trimeglamide was 50 mg/kg; this dose had a latency of 30 to 90 minutes and a duration of 2 to 6 hours. When asleep, the animals could be aroused easily by sound or touch, and they would respond in a normal manner to external stimuli. If left alone, the animals would fall asleep again within a few minutes. There were no indications of skeletal muscle involvement, and no gross abnormalities were detected in neurological examinations. Effects on blood pressure and heart rate were also absent. Rate and depth of respiration remained unchanged.

Larger doses (100 mg/kg) only prolonged the soporific action in cats. In dogs, the soporific effects were also longer lasting and, in addition, some side effects appeared: emesis in about 10 percent of the animals and some muscle twitching and occasional slight ataxia. In addition, a few animals showed definite signs of hyperactivity prior to falling asleep. Raising the dose to 500 mg/kg did not increase the central depressant activity in the dogs nor did it produce sleep, hypnosis, or anesthesia (1). Instead, after a brief period of drowsiness or somnolence, a stimulant effect was superimposed upon the soporific action. This state was characterized by restlessness and purposeful locomotion (even though slight ataxia was present in some animals), unusual inquisitiveness, but also some apparent disorientation. Minor obstacles such as a chair leg or a small carton would completely stop the animals, and no attempt would be made to go around or remove the obstacle. Furthermore, the animals frequently would attempt to crawl into almost inaccessible places. As far as could be ascertained, there was no impairment of vision, hearing, taste, or smell. The drug effect gradually disappeared within 2 to 6 hours.

The absence of hypnosis or anesthesia at five to ten times the effective soporific dose in dogs is rather unique and distinguishes trimeglamide from such pres-

ently used sedatives as barbiturates, chloral hydrate, methypyrrolon, ethchlorvynol, and others.

In man, single or repeated oral doses of 500 to 1500 mg caused sedation or drowsiness, or both, without any side effects in about half of over 200 patients thus tested (2). Oettinger (3) has described the effect of trimeglamide on electroencephalographic recordings. The administration of 2 to 8 mg/kg to 51 children or adults produced in the majority of patients a feeling of relaxation and pleasant tiredness. Electroencephalographic recordings showed neither spindling nor any drug-induced artifacts and no changes in alpha frequency or alpha index.

The lack of hypnosis or anesthesia and of undesirable side effects or artifacts is a distinct advantage for a sleep-inducing drug. In the case of trimeglamide, this advantage is of particular interest since the acute toxicity is very low. Dogs, cats, and mice have tolerated single oral doses of 500, 770, and 2000 mg/kg, respectively. Chronic administration to dogs (35 mg/kg day for 9 months) and rats (100 mg/kg day for 6 months) did not produce signs of drug toxicity during the test or on histopathological examination.

The prolongation of barbiturate-induced sleeping time is considered an index of general central nervous system depression. In mice, sleep induced by pentobarbital sodium (65 mg/kg, intraperitoneal) was increased from  $64 \pm 11$  to  $135 \pm 21$  minutes ( $\pm$  standard error) by premedication with 300 mg/kg of trimeglamide given orally 30 minutes before the test. With a subthreshold dose of pentobarbital sodium (30 mg/kg, intraperitoneal) a sleeping time of 13 minutes in 1/20 control mice was increased to  $36 \pm 9$  minutes in 14/40 mice premedicated 30 minutes before the test with an oral dose of 300 mg/kg of the drug. In dogs, with thiopental sodium as the anesthetic, trimeglamide, when given perorally at 20 mg/kg 30 minutes before the test, increased the sleeping time from  $20 \pm 9$  minutes to  $46 \pm 15$  minutes. No apparent effect on respiration was observed. Conversely, premedication with the same dose significantly reduced the amount of thiopental required to abolish the swallowing reflex from  $16.8 \pm 2.8$  mg/kg to  $11.3 \pm 2.9$  mg/kg in a crossover experiment with eight dogs.

Trimeglamide has anticonvulsant effects in mice against supramaximal electroshock (monophasic rectangular wave, 60 cy/sec, 8.3 msec pulse duration, 0.2 sec shock duration delivered through ocular electrodes). The oral  $ED_{50}$  of 510 mg/kg given 30 minutes before the test was about one-sixth of the acute  $LD_{50}$ . The drug resembled in this respect other general central nervous system depres-

sants such as methylparafynol, methylpyrrol, or ethchlorvynol.

To test for the development of tolerance, pentobarbital-induced sleeping time was determined in mice as described previously after a single or five daily oral doses of 300 mg of trimethylamine per kilogram. The sleeping times (ten mice/group) were  $74 \pm 10$  minutes for the control,  $174 \pm 32$  minutes after a single dose,  $112 \pm 14$  minutes after repeated doses. Thus some degree of tolerance had developed under these conditions in mice.

In dogs, trimethylamine had a mild protective effect against apomorphine-induced emesis. The  $ED_{50}$  of intravenously administered apomorphine hydrochloride was increased from  $8.3 \pm 0.6$  to  $11.4 \mu\text{g/kg}$  after three oral doses of  $36 \text{ mg/kg}$  day. No tolerance developed to this antiemetic effect during 7 months of daily drug administration.

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#### References and Notes

1. In the present discussion hypnosis is defined as a state of deep sleep from which the animals are aroused only with difficulty. However, when they are aroused, the animals appear normal but are reluctant to move around even though no ataxia is detectable.
  2. Unpublished reports from several investigators to the Medical Department, Riker Laboratories, Inc.
  3. L. Oettinger, Jr., and H. Sjaardema, *J. Nervous Mental Disease*, in press.
- \* Present address: Department of Pharmacology, University of Manitoba, Winnipeg.

14 May 1958

### Development of Resistance of Influenza B Virus to Polysaccharides

**Abstract.** Algal polysaccharide obtained from carrageenin protects 80 to 100 percent of chicken embryos against fatal infections with the Lee strain of influenza virus. This report describes the rapid emergence of a stable variant of this virus which is resistant to the protective action of this polysaccharide.

In the absence of any practical chemotherapy for viral diseases (except for the diseases caused by the agents of the psittacosis-lymphogranuloma group that are no longer classified with the true viruses), published information concerning the development of drug resistance of viruses is scarce. Ginsberg and Horsfall (1) reported the development of a variant of mumps virus resistant to the antiviral action of the capsular polysaccharide of *Klebsiella pneumoniae*, but the resistant character of this mutant did not persist after three to five passages in the absence of the polysaccharide.

Table 1. Effect of algal polysaccharide treatment in chicken embryos infected with influenza B virus (Lee strain) or with a resistant variant (infections and treatment by the allantoic route).

Viral strains	No. of $LD_{50}$ 's	Treatment*	Survivors/ total	Average survival time (days)
Parent	10	Algal polysaccharides (400 $\mu\text{g}$ )	10/10	> 10
Parent	100	Algal polysaccharides (400 $\mu\text{g}$ )	10/10	> 10
Parent	10	Saline	0/10	4.3
Parent	100	Saline	0/10	4.2
Variant	10	Algal polysaccharides (400 $\mu\text{g}$ )	0/10	4.3
Variant	100	Algal polysaccharides (400 $\mu\text{g}$ )	0/10	4.0
Variant	10	Saline	0/10	4.5
Variant	100	Saline	0/10	4.2

\* One hour after infection.

We recently observed that 40  $\mu\text{g}$  or more of algal polysaccharide derived from carrageenin or *Gelidium cartilagineum* protected 80 to 100 percent of 10-day-old chicken embryos against fatal infection with the Lee strain of influenza B virus if the embryos were treated within 8 to 10 hours after infection with 100 median lethal doses ( $LD_{50}$ ) of the virus. This offered an opportunity to study the development of variants resistant to the protective action of this polysaccharide.

In the experiments described below the algal polysaccharide was obtained by acetone precipitation of aqueous extracts of carrageenin. The viral strains employed were the egg-adapted Lee strain of influenza B virus (designated as the parent strain) and a variant of it resistant to this polysaccharide. The variant strain was produced by two passages of the parent strain in 10-day-old embryos in the presence of the algal polysaccharide at a dose (400  $\mu\text{g}$ ) which was 10 times that required to protect 80 to 100 percent of the embryos. For this purpose each tenfold dilution ( $10^{-5}$  to  $10^{-9}$ ) of the parent strain was injected intra-allantoically into ten embryos and, after 1 hour, the eggs were injected by the same route with the polysaccharide. After 48 hours' incubation at  $36^\circ\text{C}$ , the eggs were chilled and the individual allantoic fluids were tested for the presence of viral hemagglutinins.

In the  $10^{-5}$  dilution group the fluids of two of the ten eggs tested were positive, whereas none of the fluids of the eggs infected with higher dilutions of virus caused detectable hemagglutination. One of these positive allantoic fluids was passed again in fertile eggs similarly treated with the polysaccharide. At 48 hours, viral hemagglutinins were present in 10/10, 6/10, and 1/10 of the fluids from the  $10^{-7}$ ,  $10^{-8}$ , and  $10^{-9}$  dilution groups, respectively. The virus present in the positive allantoic fluid from the highest dilution group was designated as the

resistant variant; it was then distributed into several ampules and was stored at  $-60^\circ\text{C}$ .

The parent and variant strains were found to be similar with respect to virulence for chicken embryos, rate of multiplication in fertile eggs, and serological character. Their respective responses to the action of algal polysaccharide are shown in Table 1. It may be seen that treatment with polysaccharide protected all of the embryos infected with the parent strain of influenza Lee virus but that the variant strain was completely resistant to the action of the polysaccharide. There was no significant difference in the average survival times between the embryos infected with the variant strain and the saline-treated embryos infected with the parent strain. Similar results were obtained in a second series of experiments.

The persistence of the resistant character of the variant strain in the absence of the algal polysaccharide was demonstrated in two separate experiments in which it was passaged at high concentration ( $10^{5.5} LD_{50}$ ) in untreated chicken embryos every 24 hours. The drug-resistant character remained unchanged following 12 such serial transfers in the absence of the polysaccharide.

This stable polysaccharide resistance may be a useful finding in studies of viral genetics. The rapid development of the resistance indicates that any chemotherapy for influenza may be complicated by the emergence of drug-resistant variants.

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#### Reference

1. H. S. Ginsberg and F. L. Horsfall, Jr., *J. Exptl. Med.* 90, 393 (1949).
- \* Present address: Division of Biological Standards, National Institutes of Health, Bethesda, Md.

11 August 1958



# Salt Excretion by Nasal Gland of Laysan and Black-Footed Albatrosses

**Abstract.** Excretion of a liquid which dripped from the tip of the beak followed administration of salt loads. The  $\text{Na}^+$  concentration in the liquid was 792 to 856 milliequivalents per liter, almost twice that in sea water. The nasal gland may thus enable these birds to meet their need for water by drinking sea water.

Recently, Schmidt-Nielsen and his co-workers have discovered that the nasal gland of two species of marine birds, the double-crested cormorant (*Phalacrocorax auritus*) and the Humboldt penguin (*Spheniscus humboldti*), excretes salt (1, 2). The nasal gland of birds, as these authors pointed out, has been known for a long time—in albatrosses, since 1834 (3)—but its function was unknown before this recent work. We have had an opportunity (4) to observe excretion of salt by this gland in two adult Laysan albatrosses (*Diomedea immutabilis*) and three adult black-footed albatrosses (*D. nigripes*). The two species are commonly called gooney birds. These were sent from Midway Island, where they breed. Since the sexes are indistinguishable externally, the sexes of these birds were unknown.



Fig. 1 (top). Head of black-footed albatross, showing tube-nostril, opening of nasal gland below nostril, and groove on beak along which nasal excretion flows to the tip. Fig. 2 (bottom). Skinned head of black-footed Albatross, showing nasal glands. The left gland has been removed to expose its bony socket. The right gland has had the capsule around it cut along the margin for differentiation in the photograph.

The birds were fed fish and given artificial sea water to drink. Voluntary drinking of this water by the birds was observed many times. A salt load was administered by feeding to each a piece of fish in which a gelatin capsule containing 0.8 g of NaCl was imbedded. Drops of the excretion appeared at the tips of the beaks of the birds, usually within 20 to 30 minutes, but occasionally in only 8 or 10 minutes. The differences may have been due to different rates of digestion of the fish. The fluid emerged from a small opening (Fig. 1) beneath the tube-nostril which is characteristic of albatrosses and other Procellariiformes. It flowed along the groove on the beak to the tip, from which it dripped or was shaken off. The drops fell at a rate of about 10 to 20 per minute during regular flow.

Samples of the nasal excretion were obtained from unrestrained birds by holding vials beneath the tips of the birds' beaks. This was tedious, for the animals often turned their heads to watch the vials, thus causing the drops to be missed. In an effort to speed up collection, the birds were restrained, but, in this case, dripping ceased within 30 to 60 seconds. Upon release of the birds, the dripping started again, within 1 to 2 minutes, usually at a greatly increased rate.

Determinations of sodium and potassium ion concentrations in the nasal excretion and blood plasma were made with a Beckman flame spectrophotometer. These data are given in Table 1. For the Laysan albatrosses, the mean value for sodium in the nasal excretion was 836 meq/lit.; for the black-footed albatrosses, 826 meq/lit. (the difference is not statistically significant). The values for the nasal excretion are like those reported by Schmidt-Nielsen and Sladen (2) for the penguin ( $\text{Na}^+ = 726$  to 840 meq/lit.;  $\text{K}^+ = 21$  to 29 meq/lit.) rather than like those for the cormorant ( $\text{Na}^+ = 500$  to 600 meq/lit.;  $\text{K}^+ = 5$  to 24 meq/lit.). There was no detectable change in the concentrations of these ions in the blood during excretion.

The nasal glands of these albatrosses thus act, like those of the other marine birds studied so far, to remove sodium and potassium ions from the blood. They are large and are situated in bony sockets above the eyes (Fig. 2), with ducts leading to the external openings. The similarity between the excretion in the penguin and the albatross is probably related to the fact that both are entirely marine in habitat and ingest sea water either voluntarily or accidentally. The action of this gland would enable the birds to use sea water as a source of water, in spite of its hypertonicity ( $\text{Na}^+ = 420$  meq/lit.).

These albatrosses, which are large and

Table 1. Amounts of sodium and potassium ions (meq) in the nasal excretion and blood plasma of albatrosses. Blood samples were drawn before feeding of NaCl and during excretion following feeding of NaCl. ( $\sigma$ , Standard error of the mean.)

No. of samples	Na <sup>+</sup> (meq/lit.)		K <sup>+</sup> (meq/lit.)	
	Range	$M \pm \sigma$	Range	$M \pm \sigma$
Nasal excretion				
7	792-856	829 $\pm$ 7.3	20-28	24 $\pm$ 1.0
Blood plasma before excretion				
4	162-171	167 $\pm$ 1.9	4.9-7.0	5.7 $\pm$ 0.4
Blood plasma during excretion				
5	159-170	164 $\pm$ 2.0	4.6-6.0	5.4 $\pm$ 0.3

docile, should make good subjects for studies of the action of this gland and its relationship to the water and ionic balance of marine birds. Hubert and Mable Frings have used the knowledge of the action of this gland to develop a method (5) for keeping these birds in captivity in apparently normal health.

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4. These studies were aided by a contract between the Office of Naval Research, Department of the Navy, and Pennsylvania State University (NR160-464). The birds were shipped by air through the cooperation of the Bureau of Aeronautics, Department of the Navy, and naval authorities on Midway Island, to whom we wish to express our appreciation. This is paper No. 2285 in the "Journal Series" of the Pennsylvania Agricultural Experiment Station.
5. A report on this method is in preparation.

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## Correlation of Drug Penetration of Brain and Chemical Structure

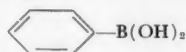
**Abstract.** A study has been carried out on the permeability of the brain and a brain tumor to certain aromatic boronic acids with regard to their use in the neutron capture therapy of gliomas. The penetration of the brain by these compounds is discussed as a function of chemical substituent and benzene-aqueous partition coefficient.

The possibility of destroying differentially a group of neoplastic cells adjoining normal cells is presented by the nature of the reaction when boron-10 or lithium-6 captures a slow neutron (1). A large amount of energy liberated is shared between the two heavy fragments



evolved, the smaller of which is an alpha particle. In the case of the nonradioactive boron-10, the 2.5 Mev available (2) will propel the alpha particle only 9  $\mu$  in tissue (3) from the site of the reaction. In view of this short range, the lethal effect of the radiation is confined to the region of the cell containing the capturing atom of boron—hence the search for a boron-containing substance which will preferentially localize in tumor.

Since normal brain possesses a pronounced barrier mechanism not present in its tumors (4), the study described in this report (5) was motivated by an effort to learn what features a molecule should have in order to be selectively retarded in passage from blood to brain or accelerated in passage from blood to brain tumor. A series of molecules differing but little from one another in size and chemical configuration has been synthesized in order to minimize the variables. The basic moiety was phenylboronic acid:



Eight monosubstituted derivatives, most of them known compounds, were prepared for this study. These compounds were administered intraperitoneally to C3H mice bearing subcutaneously transplanted gliomas. The boron content (6) of 50 mg each of five tumor and five brain samples was determined at the several stated intervals after injection. Table 1 gives the average of these analyses in micrograms of boron per gram of tissue for brain and tumor at each of these stated times.

The localization factor for boron, the ratio of tumor to brain content of the element, is a measure of the relative rate of transfer between blood and the two tissues in question.

In a parallel study, approximately 10 mg of each of these nine compounds was distributed between 50 ml of a phosphate-buffered aqueous medium of pH 7.2 and 50 ml of benzene. The purpose of this study was to correlate the penetration of the brain by these drugs with their partition between benzene and water. Since benzene is a lipid solvent, the relative concentration of the compound in this medium could be a measure of lipid solubility. Many investigators have proposed that the penetration by drugs of the brain is mainly a function of their lipid solubility (7). By use of these monosubstituted phenylboronic acids, this theory could be tested. In addition, it was considered that the effect of an individual group on a molecule in enhancing or diminishing its penetrability could be determined and that this might aid in the design of effective

tive neurotropic drugs on the one hand and tumor-seeking drugs on the other.

The compounds listed in Table 1 may be divided into three distinct groups. There are three compounds, *m*-carbamido-, *m*-carboxy-, and *p*-carboxyphenylboronic acids in the first group. All show

tumor-to-brain localization factors of greater than 3, with a maximum attained 30 minutes to 1 hour following the injection. These three compounds likewise had a water-to-benzene partition coefficient greater than 50 to 60. They exhibited no effect on the central nervous

Table 1. Boron concentrations and ratios.

Time of sacrifice (min)	Concn. of B ( $\mu\text{g/g}$ of tissue)		Localiza- tion factor (tumor/ brain)	Concn. of B ( $\mu\text{g/ml}$ of solvent)		Partition coefficient (aqueous/ benzene)
	Tumor	Brain		Aqueous medium	Benzene	
m-Carbamidophenylboronic acid (dose: 35 $\mu\text{g/g}$ )						
15	12	2	6.0			
30	18	2	9.0			
60	24	4	6.0	10.9	< 0.2	> 54
120	18	6	3.0			
180	15	6	2.5			
m-Carboxyphenylboronic acid (dose: 140 $\mu\text{g/g}$ )						
15	57	10	5.7			
30	63	8	7.5			
60	61	10	6.1	12.1	< 0.2	> 60
120	60	13	4.6			
180	55	13	4.2			
p-Carboxyphenylboronic acid (dose: 140 $\mu\text{g/g}$ )						
15	44	11	4.0			
30	68	10	6.8			
60	62	8	7.7	11.4	< 0.2	> 57
120	47	9	5.2			
180	38	8	4.7			
p-Methoxyphenylboronic acid (dose: 35 $\mu\text{g/g}$ )						
15	29	44	0.7			
30	33	40	0.8			
60	34	38	0.9	13.1	2.5	5
120	36	34	1.1			
180	30	26	1.2			
Phenylboronic acid (dose: 35 $\mu\text{g/g}$ )						
15	34	51	0.7			
30	34	44	0.8			
60	29	30	1.0	14.4	2.3	6
120	26	29	0.9			
180	34	40	0.8			
o-Nitrophenylboronic acid (dose: 35 $\mu\text{g/g}$ )						
15	25	41	0.6			
30	29	41	0.7			
60	26	36	0.7	12.6	1.9	7
120	41	49	0.8			
180	43	50	0.9			
p-Chlorophenylboronic acid (dose: 35 $\mu\text{g/g}$ )						
15	13	69	0.2			
30	19	66	0.3			
60	33	57	0.6	6.9	5.6	1
120	32	58	0.6			
180	30	51	0.6			
p-Tolylboronic acid (dose: 35 $\mu\text{g/g}$ )						
15	18	53	0.3			
30	20	44	0.5			
60	30	37	0.8	8.0	5.2	2
120	31	25	1.2			
180	29	18	1.6			
m-Aminophenylboronic acid (dose: 35 $\mu\text{g/g}$ )						
15	25	21	1.2			
30	32	26	1.2			
60	28	23	1.2	12.4	< 0.2	> 62
120	22	17	1.3			
180	16	13	1.2			

system as judged by gross observations of the animal behavior, even in large doses.

In the second category are *o*-nitro-, *p*-methoxy-, and the unsubstituted phenylboronic acid. These three compounds had a localization factor of nearly 1, but in most cases the brain had a slightly higher boron content. These compounds produced an immediate depressant action upon the animal's spontaneous activity and responsiveness to stimuli, and soon the animals were lying flaccid and supine, unresponsive to surgical operations. The aqueous-benzene partition coefficient was from 5 to 7.

In the final category are two compounds, *p*-tolylboronic acid and *p*-chlorophenylboronic acid. At the standard dose of 35 µg per gram of mouse, the compounds were highly toxic, and the LD<sub>50</sub> was approached. Coma in these animals was often accompanied by generalized twitching of the limbs. Initially, both showed a tumor-to-brain localization of 0.2 to 0.3, and thus their behavior suggests that they encounter, not a barrier slowing their penetration into brain, but an avenue facilitating it. The water-benzene partition coefficient was from 1 to 2. It is apparent that these compounds which show maximal effects on the central nervous system and greater concentration in the normal brain relative to tumor do concentrate to a greater extent in the lipid solvent, benzene, whereas those which show no obvious effect on the central nervous system and low concentration in the brain have a much higher partition coefficient in an aqueous rather than in a lipid phase.

Initially, *p*-tolylboronic acid showed a localization factor 0.3, but gradually this ratio was reversed, and after 3 hours the tumor concentration was nearly twice the brain concentration. Methyl groups attached to an aromatic nucleus are readily oxidized in vivo to a carboxyl group—for example, toluene is transformed on ingestion to benzoic acid (8). If this type of conversion occurs with *p*-tolylboronic acid, then *p*-carboxyphenylboronic acid would be formed and this reversal would be understandable. *p*-Chlorophenylboronic acid, on the other hand, maintained a localization factor of 0.6 even after 3 hours.

An exception to this three-category division would appear to be *m*-aminophenylboronic acid. This compound shows an effect on the central nervous system only at doses of 70 µg per gram of mouse and yet the boron localization factor is nearly 1 and the aqueous-benzene partition coefficient is greater than 60. It is conceivable that this compound might be intermediate between groups 1 and 2 or possibly that a principle other than lipid solubility is involved.

In summary, it can be stated that in-

creased solubility in a lipid solvent is an important measure of the penetration of the brain by a drug. Of the compounds which were examined, introduction of a methyl or a chloro substituent into an aromatic nucleus definitely enhanced the penetration of a molecule into the brain, while a carboxyl or carbamido substituent markedly inhibited its entrance.

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### Acute Infection of Mice with Smith Strain of *Staphylococcus aureus*

**Abstract.** Two serologically distinct variants found in a unique strain of staphylococcus produce coagulase and are phagocytized, but only one is virulent to mice. Only virulent cocci grow rapidly within leukocytes. Leukocyte destruction by the virulent strain and release of many phagocytized cocci precedes mouse death. The leukocidal agent may be delta-hemolysin.

The Smith strain of *Staphylococcus aureus* (1), which was isolated in 1930 by Dubos and briefly described by Smith and Dubos (2), is an unusual organism. We have studied in detail the mouse infections produced by this strain because it is unique. An examination of the strain showed that there were at least two cellular types in the broth culture. This differentiation was most readily made when the plasma soft agar reaction described by Finkelstein and Sulkin (3) demonstrated the presence of both diffuse and compact colonies in the culture. Although both types of Smith colonies produce coagulase, as determined by the tube test, only the diffuse colony in the plasma soft agar was virulent to mice. We have

encountered no other staphylococcus strain with such capacity for inducing an acute infection in mice when injected by the intraperitoneal route. We have found no other strain of coagulase-positive staphylococcus which produced diffuse colonies in soft agar containing normal plasma or serum.

Smith and Dubos (2) stated that the strain produced pigment, was coagulase-positive, and was phage type 44A/42E. We have observed that the strain readily produced delta-hemolysin. Very rarely one may observe a colony producing beta-hemotoxin, but most colonies did not produce demonstrable alpha- or beta-hemotoxins on sheep washed-blood-cell agar plates after incubation in 10 percent carbon dioxide. We have never observed the production of staphylokinase or bacterial protease by the organism, as judged by lysis of fibrin formed around colonies on fibrinogen agar plates. The intraperitoneal median lethal dose (LD<sub>50</sub>) of the diffuse-colony culture in Swiss albino mice was approximately  $4 \times 10^6$  viable cells per mouse when injected as a broth suspension, but, with 0.5 ml of 5 percent hog gastric mucin, the LD<sub>50</sub> was about 580 cells per mouse. Other strains of *Staphylococcus aureus* isolated from lesions of human beings and of laboratory animals showed an intraperitoneal LD<sub>50</sub> of  $1 \times 10^6$  viable cells in mucin, but did not consistently cause death when  $1 \times 10^9$  viable cells were injected without mucin.

The presence of diffuse and compact coagulase-positive colonies in the Smith strain cultures was confirmed when the strain was sent to Finkelstein and Sulkin (4). The latter described their observations and noted that the Smith compact isolate was agglutinated with absorbed Group II (Cowan) antiserum and was lysed by phage type 44A. The diffuse-colony isolate, however, did not agglutinate with Groups I, II, or III absorbed antisera, nor was it lysed by type 44A phage. This suggested that the two cellular types were serologically distinct and that the compact type contained an antigen not found in the diffuse cell.

We had observed that the separation of diffuse and compact colonies of the Smith strain by the plasma soft agar also separated the mouse-virulent colonies from the mouse-avirulent. Peritoneal washings from any mouse dying from infection by the Smith strain showed only diffuse-type colonies in plasma soft agar. Each colony type, when isolated and grown through four or five broth-to-broth transfers without reisolation, showed the presence of a few cells of the other type colony. Without reisolation, a compact-colony broth culture might contain a few diffuse-type cells. Large challenge doses of the compact-type cultures produced death in an occasional mouse, but peri-

Table 1. Growth of compact- and diffuse-colony variants of *Staphylococcus aureus* (Smith) and colonies of *Staphylococcus aureus* (193) in normal mouse serum and in the mouse peritoneum.

Time (hr)	Growth of Smith strain of <i>S. aureus</i> in normal mouse serum		Growth of Smith strain of <i>S. aureus</i> in mouse peritoneum		Growth of <i>S. aureus</i> (193) in mouse peritoneum
	Viable diffuse cells/ml of serum	Viable compact cells/ml of serum	Viable diffuse cells/ml of exudate	Viable compact cells/ml of exudate	Viable (all compact) cells/ml of exudate
0	$8.3 \times 10^4$ *	$5.2 \times 10^4$ †	$4.2 \times 10^6$	$1 \times 10^6$	$2.4 \times 10^6$
4			$4.6 \times 10^6$	$2 \times 10^6$	$3.3 \times 10^6$
8			$> 2 \times 10^6$	$1.3 \times 10^6$	$8.6 \times 10^6$
10			$> 2 \times 10^6$	$2 \times 10^4$	$6.6 \times 10^6$
24	$1.4 \times 10^7$ *	$1 \times 10^7$ †	All mice dead (at 12 hrs)	$< 1 \times 10^5$ (All mice survived)	$< 1 \times 10^5$ (All mice survived)

\* All diffuse colonies in plasma soft agar. † All compact colonies in plasma soft agar.

toneal washings from such mice, suitably diluted in plasma soft agar, have always shown all colonies to be diffuse, and indicate an in vivo selection of the few diffuse cells present in large volumes of older compact-type cultures.

Both the diffuse-colony and the compact-colony isolates of the Smith strain grew equally well, as indicated by plate counts, when incubated in normal human or mouse serum over a 24-hour period, but they developed at very different rates within the leukocytes in the mouse peritoneum. One was able to observe the progress of infections due to challenges of diffuse and compact isolates when peritoneal exudates of mice injected with the Smith strain were periodically sampled and stained with Wright stain. In the mouse peritoneum there was a prompt leukocytosis and a prompt phagocytosis of staphylococci, whether the challenge was of compact- or diffuse-colony origin. The phagocytized organisms from compact-colony isolates were viable, but there was little growth, as judged by plate counts and by estimation from stained-slide preparations.

What we observed with the diffuse-colony infection was quite different. There was a marked and consistent proliferation of the diffuse-colony staphylococci within the leukocytes for 8 to 12 hours, depending upon the challenge dose. During the interval between the eighth and twelfth hour, in the mice receiving the diffuse-colony challenge, there was an abrupt appearance of overwhelming numbers of extracellular staphylococci, and the mice died within the next 20 to 40 minutes. When a similar "shower" of extracellular organisms was observed in mice receiving large challenge doses of compact cultures of the Smith strain, these mice died, and examination of their peritoneal exudates showed that the organisms were all dif-

fuse cells. Other strains of coagulase-positive staphylococci tested, developed as compact colonies in plasma soft agar, grew well in normal serum but, like the compact Smith strain, did not show significant growth in the leukocytes in the mouse peritoneum, although they remained viable for many hours. These relationships are shown in Table 1.

Rogers and Tompsett (5) have indicated that the disappearance of white blood cells from in vitro staphylococcus-leukocyte suspensions and the appearance of extracellular staphylococci might be due to the production of the leukocidin which Valentine (6) described as being lytic for the leukocytes. Jackson and Little (7) and Gladstone and van Heyningen (8) believe that this lytic leukocidin is delta-hemolysin.

Both variants of the Smith strain produced delta-hemolysin. Both were phagocytized by the leukocytes, and both remained viable for 12 hours in the white blood cells. The outstanding difference between the two isolates was their serological dissimilarity and the ability of the diffuse-type organism to develop readily within the leukocytes. Intracellular growth and production of leukolytic concentrations of delta-hemolysin without interference of inhibitory agents within the mouse leukocytes could then account for the sudden appearance of diffuse-type extracellular staphylococci. These organisms showed no evidence of clumping in the peritoneal exudate but disseminated freely. Sudden release of the organisms into the peritoneum, together with any toxic products formed by the staphylococci or lysed leukocytes, would account for the subsequently fatal outcome of the infection. Since the growth of the compact variant was inhibited within the white cells in the mouse peritoneum, there might not be a lytic concentration of delta-hemolysin produced to destroy

the white cells. Dissemination of staphylococci and their toxic products hence would not take place.

Death of mice following intraperitoneal injection of very large challenge doses of other strains of coagulase-positive staphylococci suggests that the inhibitory activity within the phagocytes may be overcome by large numbers of cocci, or that incubation of the large number of viable phagocytized staphylococci may produce enough of the leukolytic agent to lyse the white cells and release lethal products to produce the delayed toxic death observed. The peritoneal washings of mice dying from large challenge doses of these strains show no diffuse colonies in plasma soft agar.

Further study of the influence of delta-hemolysin and of specific antibodies upon staphylococcus infection is in progress. The study of rare staphylococcus mutants not ordinarily encountered by the general population of experimental animals should help to elucidate the role of coagulase and of inhibiting agents in infection.

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#### References and Notes

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11 August 1958

#### Fractional Escape and Avoidance on a Titration Schedule

**Abstract.** Rats were shocked, continuously or intermittently, by an electrical stimulus whose intensity increased by one step every 20 seconds. Each time the rat depressed a lever in the experimental chamber, shock intensity was decreased by one step. Lever-pressing was maintained on such a program, with both continuous and intermittent delivery of shock.

Operant conditioning techniques can be used to acquire information about thresholds, or about the intensity or amount of a stimulus or reinforcer that will be tolerated or preferred. Here we report results obtained by a technique

that permits one to gauge the tolerance of a subject to electric shock (1). It is related to those used by Békésy, Blough, and Lindsley to measure, respectively, auditory thresholds, visual thresholds, and depth of sleep (2).

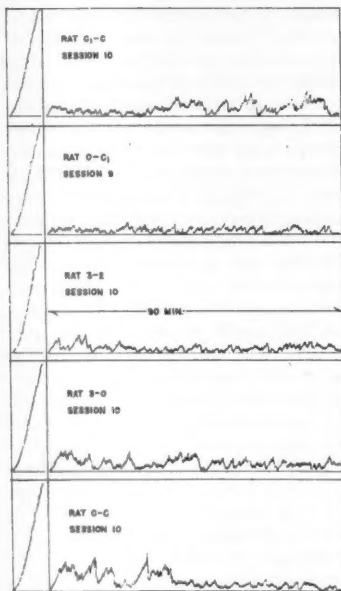


Fig. 1. Records for five animals on the fractional-escape schedule. The inset to the left of each record indicates the programmed rate of increase—that is, the rate at which the shock level would rise if the rat did not respond.

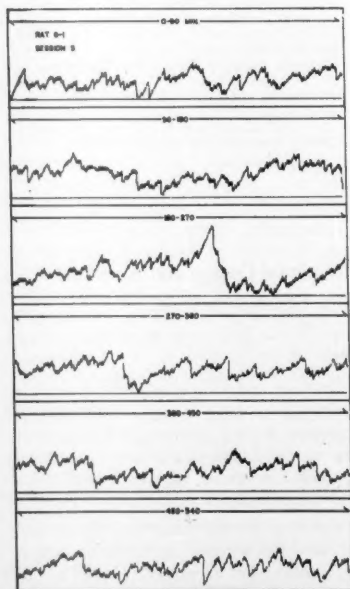


Fig. 2. Complete record of a 9-hour session on the fractional-avoidance program.

The technique employs a constant current shock stimulator whose output can be increased or decreased in discrete steps (3). The 30 steps between the minimum and maximum values of the output current are selected by a two-way stepping relay.

A pulse emitted by a timer activates the "increase" relay so that an increment in the shock level occurs every  $t$  seconds. For the data reported here,  $t$  was 20. The shock current is delivered to a floor of stainless steel rods in the experimental chamber, which is enclosed in a sound-deadened box (4) in a room adjacent to the one that contains the programming and recording apparatus. Each time the rat presses a lever in this chamber, a pulse is delivered to the "decrease" relay, and the stimulator output is reduced by one step. From such a program, which we have labeled a "titration schedule," we get a continuous assay of the rat's tolerance to electric shock. A recording millivoltmeter indicates the output of the stimulator.

A half-wave 60-cycle signal is the form in which the shock is delivered, with the wave form approximating a square wave. Two ranges were employed. The higher varied from 0.07 to 0.72 ma; the lower varied from 0.06 to 0.41 ma (5).

The titration method has been used in two different ways. In one, which might be called fractional escape, shock was applied continuously to the grid. Lever-presses reduced the intensity of this shock. The lower shock range was always used. In the other method of programming, which might be called fractional avoidance, a brief shock was delivered every 20 seconds, with each succeeding shock a step higher than the last. If the rat pressed the lever between shocks, the next shock he received was less intense by a number of steps equal to the number of responses he had made. Thus, responses did not avert but merely reduced the strength of the forthcoming shock. The lower range was used with three rats, the higher with two.

Five adult Wistar strain male albino rats have been studied with each method. All had been given preliminary experience on an avoidance schedule in which each lever-press postponed a brief shock (6).

Sample records from each of the five animals trained on the fractional-escape schedule are shown in Fig. 1. These represent the ninth or tenth 90-minute sessions for these subjects. The task was learned very quickly by the rats we used, and variability rapidly decreased with experience. At the stage of training shown in the figure, the amount of current tolerated by the rats did not shift very much within a session, nor did it vary appreciably from session to session. The distribution of responses in the 20

seconds between pulses to the "increase" relay was recorded in 2-second intervals. No single interval showed a preponderance of responses.

Each session on the fractional-avoidance schedule lasted for 9 hours. A representative record for a complete session is shown in Fig. 2. As in the fractional-escape procedure, no within-session or session-to-session trends in tolerance level could be discerned. The distribution of responses between shocks was recorded in 2-second intervals. Responses were most frequent in the first interval after the shock and dropped sharply afterward. Session-to-session changes consisted of slight decreases in the number of responses in each interval was computed for the fifth session with the data from all five animals combined. These percentages were as follows: 33, 17, 10, 7, 6, 6, 6, 5, 5, 5.

Behavior on the fractional-escape schedule demonstrates that lever-pressing is maintained by fractional reductions in the intensity of a continuously applied noxious stimulus. Behavior on the fractional-avoidance schedule demonstrates that lever-pressing is maintained when the consequence of a response is a reduction in the intensity of a forthcoming shock.

The reinforcement for continuing to perform on the fractional-escape schedule is fairly clear, since each response produces an immediate decrease in shock intensity. What precisely motivates responding on the fractional-avoidance schedule is more obscure, although the response distribution indicates that most of the responses are elicited by the shock itself or by some state which the shock induces.

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#### References and Notes

1. This work was supported by grants from the United States Public Health Service [B-865 (C2)] and from the Institute for the Study of Analgesic and Sedative Drugs.
2. G. V. Békésy, *Acta Oto-Laryngol.* 33, 411 (1947); D. S. Blough, *J. Exptl. Anal. Behavior* 1, 31 (1958); O. R. Lindsley, *Science* 126, 1290 (1957).
3. The stimulator was designed by G. N. Webb, biophysics division, department of medicine, Johns Hopkins University School of Medicine. A report is now in preparation.
4. The sound-deadened box used in this study was manufactured by Foringer and Co., Rockville, Md.
5. Measured by a Hewlett-Packard 400 AB vacuum tube Voltmeter across a 100 kohm load. This instrument measures the average value of the wave. Because of the characteristics of the vacuum tube used in the stimulator, the first few steps are smaller than the others.
6. M. Sidman, *Science* 118, 157 (1953).

15 July 1958



## Increase in Locomotor Activity Following Shielding of the Parietal Eye in Night Lizards

**Abstract.** The number of movements of matched groups of night lizards in a photothermal gradient was recorded over periods of weeks. The placement of an aluminum foil shield over the parietal eye in one group was followed by an increase in activity over the control group.

Stebbins and Eakin (1) have demonstrated behavioral changes in several species of iguanid lizards following ablation of the parietal eye, compared to sham surgery. Increases in exposure to light and in distance moved from point of first capture in the field were noted. Incidental observations suggested that an increased restlessness accompanied these effects. A similar response to light could be induced by inserting a small aluminum-foil shield over the parietal eye through a slit in the deciduous *stratum corneum* of the interparietal scale. Placement of the foil to one side of the "eye" afforded a control. The shielding technique has been employed in the present study to determine whether the parietal eye exerts a measurable influence on locomotor activity.

Desert night lizards, *Xantusia vigilis vigilis*, were collected in Kern County, California, in the winter and spring of 1957-1958. They were maintained at room temperature (20 to 25°C) and supplied periodically with water and *Tenebrio* larvae. There was no feeding immediately before or during activity tests. Water was supplied on the day before each of the testing phases of an experiment.

Two spring-balanced lever actographs (2) made of balsa wood recorded locomotor activity. Each activity chamber provided a space 46 by 9 by 2 cm for movement of the lizards. The central part of the cover was of transparent Saran wrap, 30 by 9 cm; the ends were shaded with balsa wood, 8 by 9 cm. A photothermal gradient was produced by a 100-watt light bulb with reflector over the fulcrum end, about 10 cm above the cover. Illuminance, as measured with an exposure meter (3), gave direct light readings of 0.5 and 5, as transmitted to the two shaded areas, and of 1.2 to 1200 under the transparent part of the cover. The temperature extremes of 17° and 41°C, maintained constant within 1.5°C, exceeded the range favorable for activity, to judge from field microclimate studies. The apparatus was situated in a part of a refrigerated room kept at 14° to 16°C. Observations of the activity chambers were through one-way glass. The actograph scribes were adjusted for a sweep of 15 cm, with 10 g at 47 cm from the fulcrum. Recordings were made on a long-paper kymograph moving at 0.308 cm/min. Each vertical line showing an angular displacement, regardless

of amplitude, was counted as a locomotor movement.

Innate differences in locomotor performance of two matched groups of lizards were determined first. Before the establishment of this control, baseline aluminum-foil shields, 1 mm square, had been inserted into a position to one side of the parietal eye. For these and subsequent manipulations the lizards were placed under brief cold anesthesia by embedding them in crushed ice. Activity was recorded after 12 to 20 hours in the chamber. A test of activity made before the control operation in one experiment (Fig. 1, experiment 3, May) indicated

that the operation did not alter markedly the animals' subsequent locomotor performance.

The group that had established itself as the less active was selected for experimental shielding, and the foil was maneuvered into position over the "eye." In the more active group the foil was moved to a different control position. Further activity was recorded for about two weeks. The experimental and control conditions were then reversed in the two groups, and measurement of activity was resumed for about 10 days, until the termination of the experiment.

A total of 50 lizards have been tested

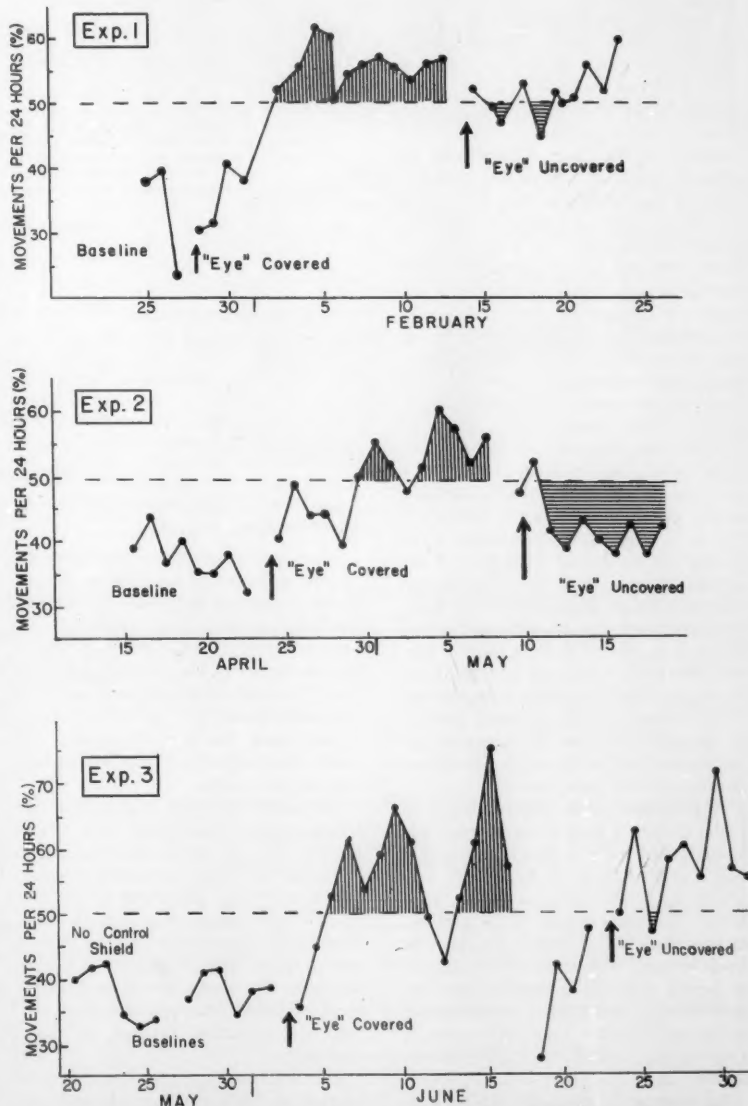


Fig. 1. Locomotor performances of groups of lizards with manipulations of a shield over the parietal eye. Scores are relative to those of matched groups whose percentage scores are not shown, forming points equidistant from, but on the opposite side of, the 50-percent line. Shaded parts emphasize activity favoring experimental groups over controls.

in three experiments; in each experiment a different set of lizards was used. Tests conducted on 97 days have yielded records of over 107,000 movements.

The locomotor movements of the initially less mobile groups have been plotted in percentage relative to the initially more active matched groups for periods of 24 hours (Fig. 1). Indications of an increase in activity of the experimental group appear in 2 to 3 days after the first operative procedure. A shift in favor of the experimental group, reversing the preceding baseline relationship, tends to appear within 6 days. Under the limitations of the experiment the shift in relative activity may persist, with temporary setbacks, for 8 to 11 days.

A satisfactory statistical model for the data is not available. Use of the chi-square test seems to indicate that the first shielding resulted in activity differing from the baseline performance at a level of high significance ( $P < 0.001$ ) in each of the three experiments; the control operation during the establishment of the baseline in May, experiment 3 (Fig. 1) did not appear to induce a significant difference in activity ( $p > 0.10$ ). But the lack of independence of the successive scores renders the chi-square test inappropriate.

Although increase in activity following the first shielding of the "eye" seems to be clearly evident, the attempts at reversal in the terminal phases of the experiment were not uniformly successful. A diminished response would not be unusual in animals approaching a state of starvation. To avoid deaths in the last testing phase, the number of individuals had to be reduced, in experiments 2 and 3, from 18 to 14 and from 12 to 8 per set, respectively. A set of 20 lizards was carried through experiment 1 in fairly good condition, but the activity reversal was only slight and did not seem to persist. The positive response in experiment 2 is opposed by the failure in experiment 3. The latter can be attributed perhaps to the small number of animals—four per group—and to the somewhat greater duration of the experiment.

A pulsation in the relative scores in cycles of 3 to 5 days is noteworthy. Examination of the raw data indicates that this is related to bursts in activity, primarily in the experimental groups; such bursts of activity appear to be periodic escapes from the decline in activity that tends to occur with time. This finding is in accord with the contention that the parietal eye, acting as a photothermal radiation dosimeter, may play a role in a homeostatic mechanism that modulates activity (1, 4).

An increase in metabolic rate following ablation of the parietal eye has been reported for *Anolis* (5). Hypertrophy and hyperplasia of the thyroid may follow parietectomy in iguanid lizards

(1) and pineal ablation in the guppy, *Lebistes* (6). An increase in locomotor activity following a shielding of the parietal eye, a part of the pineal complex, is consistent with these other findings (7).

ROBERT GLASER

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University of California, Berkeley

#### References and Notes

1. R. C. Stebbins and R. M. Eakin, *Am. Museum Novitates* 1870, 1 (1958).
2. J. S. Szymansky, *Arch. ges. Physiol. Pflüger's* 158, 343 (1914). The apparatus used was modified from one constructed and contributed for this work by Dr. R. C. Stebbins.
3. The exposure meter used in this study was a Weston-Universal Master, model 715.
4. A report on the role of the parietal eye in 24-hour endogenous locomotor rhythms is in preparation.
5. H. J. Clausen and B. Mofshin, *J. Cellular Comp. Physiol.* 14, 29 (1939).
6. O. Pflugfelder, *Wühelm Roux' Arch. Entwicklungsmech. Organ.* 148, 463 (1956).
7. I am indebted to Dr. R. C. Stebbins for providing the impetus for this study and for helpful advice throughout its conduct. I also wish to thank Drs. R. M. Eakin, F. Evans, and W. B. Quay for comments on the manuscript, Dr. E. L. Scott for advice on statistical matters, and Gene Christman for aid on the preparation of the graph.

21 July 1958

#### Use of Borosilicate Glass in Ozonizer Tubes

**Abstract.** The surfaces of borosilicate glass deteriorate in the presence of ozone. The formation and accretion of silica particles in the glass ozone generating tube of a laboratory ozonizer, of the silent discharge type, are responsible for electric breakdown at high secondary voltages on the transformer.

Numerous publications describing the conditions requisite for constant-output ozone production by means of the silent discharge method have appeared. Although a "soft" soda-lime glass is recommended for construction of discharge tubes, through which oxygen or air to be ozonized is passed (1), use of Pyrex borosilicate glass has become popular for ozone generators of both homemade and commercial origin.

The ozone generator employed in this laboratory was constructed with a discharge tube of Pyrex glass concentric about an inner tube containing a water-cooled electrode, connected to the secondary high voltage of a variable transformer. The outside of the discharge tube was wrapped with aluminum foil, connected to the transformer ground. Dried air was passed through the discharge tube and circulated through an ozone chamber.

This apparatus was employed successfully in the determination of ozone resistance of elastomeric materials for a period of about 10 years. Recently, electric breakdown at secondary voltages above 7500 volts was observed. Lowering

the secondary voltage below this value resulted in resumption of normal silent discharge.

Examination of the glass discharge tube revealed the formation of a powdery scale on the surfaces exposed to the air stream. In some cases, particle accretion had built a bridge partially or entirely across the tube. Replacement of the discharge tube led, of course, to normal operation of the ozone generator.

It was suspected that this powdery substance was an organic material, perhaps derived from the Tygon connections in the air line of the apparatus. It proved, however, to be insoluble in, and unaffected by, organic solvents or hot nitric or chromic acid. Spectroscopic analysis determined the presence of silicon and trace quantities of iron and sodium and the absence of magnesium, calcium, potassium, aluminum, or boron. A routine silica determination showed that the material contained 98 percent of silica. Microscopic examination disclosed microcrystalline particles and aggregates. That the observed silica deposits and growths were responsible for breakdown at high applied potential is evident, as is their origin from the glass of the discharge tube. It is the reason for such deposits occurring that is mysterious.

Examination of fragments of the glass surface revealed a powdery crust of silica, unevenly distributed in thickness. The material, in some spots, had formed stalactites extending into the air gap in the discharge tube. The effect of these stalactites, aside from reducing the distance of the air gap, thereby lowering the threshold voltage at which an arc would form, is to provide focal points at which charged particles will collect. Hence, point discharges may be expected to occur at these stalactites at very much lower voltages than those customarily needed for formation of an arc across the air gap.

The mechanism of the formation of silica scale under these conditions, and the particle build-up of this scale, should prove of interest for further study. We are, at present, unable to suggest any explanation for this phenomenon. It is felt, however, that these observations may be of interest, considering the widespread use of the ozone generator as an analytical tool (2).

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#### References and Notes

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2. We wish to thank Dr. John Young of this laboratory for the spectroscopic analysis that he kindly provided.

13 August 1958

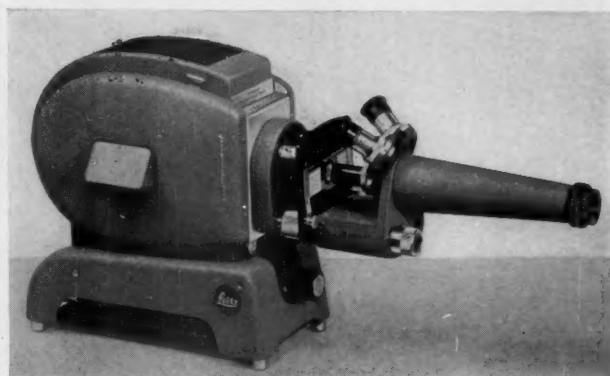
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(Continued from page 1534)

are made. On the contrary, my conclu-  
sions are not based on the results at these  
low levels. They stem from the extrap-  
olation of tumor data from mice  
through cats and dogs to man, and from  
comparisons of radium and strontium-90  
toxicity in mouse and man.

In point 2 Moos objects that the ex-  
perimental design is inadequate to dem-  
onstrate a threshold dose. That is cer-  
tainly true. However, the design is  
adequate for the intended purposes of  
the experiment—namely, to examine the  
effects of a range of doses and to investi-  
gate the shape of the dose-response curve.

One consistent difficulty in assessing  
the fallout situation is exemplified in  
point 3 of Moos's letter. The first sen-  
tence is one with which any intelligent  
person could agree wholeheartedly. The  
second sentence is a consequence of the  
charged, emotional approach so often  
apparent in discussions of the hazards of  
fallout. This attitude has unconsciously  
influenced many interpretations of radio-  
biological data. We need honest, objec-  
tive, unemotional evaluations of the ex-  
perimental results, which can then be  
applied to problems of world-wide con-  
tamination. It is very important that  
concern over these problems not be per-  
mitted to distort the appraisal of the  
experimental results.

Moos has suggested that I temper my  
conclusions. None of the animal data  
have produced linear dose-response  
curves. The obvious conclusion is not  
"that a linear dose-effect relation is less  
probable than a nonlinear relation" but  
that the relationship probably is not  
linear. Regarding the evidence for a  
threshold, I agree that the only justified  
conclusion at this time is that a threshold  
might exist. I so stated in my article.

Roth's reaction to the opening para-  
graph of "Mice, men, and fallout" beau-  
tifully illustrates one of the primary  
reasons for that article's having been writ-  
ten. Too many of us expect the distin-  
guished authority in some specialized  
field to be an unquestioned authority in  
all fields.

It has been objected that not enough  
animals were used to predict events that  
might happen one time in a few hundred  
thousand. This is certainly true. If Roth  
will reread the third paragraph of the  
article in question, he will find that my  
objective was not to test such frequen-  
cies but to examine the two major as-  
sumptions upon which the previous pre-  
dictions of damage from fallout have  
been based. The 960 mice provided dose-  
response curves with characteristics con-  
trary to these two assumptions. That is,  
they are not linear, and they suggest that  
a minimum dose must be exceeded be-  
fore the response is manifest. Conse-  
quently, extrapolations along straight  
lines from effects at moderate or high  
doses to no effect at no dose are unwar-



ranted. Our best information, based on experimentation rather than speculation, is that "... the present contamination with strontium-90 from fallout ... is extremely unlikely to induce even one bone tumor or one case of leukemia."

Roth calls attention to the very short life span of the mouse contrasted to that of man. This difference, along with the great dissimilarity in size, is the main obstacle to transferring mouse data directly to man. He will note, in the tentative extrapolations given in Fig. 5 of the article, that both of these factors have been taken into account.

Apparently Dunn and Dobzhansky feel that my article should have encompassed all of radiobiology. On the contrary, it was deliberately limited to one small aspect of this subject—namely, considerations of the methods that have been used and that can be used to predict the consequences to exposed individuals of low levels of radiation. A discussion of inheritable damage was not pertinent, and I expressly stated that the exposed generation only would be considered. If one announces that he is going to investigate the effects of temperature upon mitosis, for example, should he be accused of "willful neglect" if he does not include the effects of temperature upon gene mutation? I have had no experimental experience with radiation genetics, and it would be presumptive for me to pose as an authority on that subject. I am confident that the geneticists themselves will eventually be able to tell us whether the linear relationship between gene mutation and exposure holds at doses lower than 25 roentgens.

Dunn and Dobzhansky say that I have assumed "that the main danger of radiations in man's environment lies in their effects on the individuals exposed." There is no basis in my article for this statement. The sentences they quoted were not intended to justify the omission of a discussion of genetic consequences, as they suggest. These quotations merely describe the kind of changes that are most apparent and most easily measured in exposed animals.

I agree wholeheartedly that the data I presented have no bearing on the problem of radiation exposure and germinal mutations. It also was not my purpose to discuss somatic mutations or possible mechanisms of carcinogenesis. Why should a reader be surprised that these subjects were not covered? I also did not include any mention of the effect of radiation upon the sexual behavior of *Paramecium*.

It is difficult to understand how two distinguished scientists could so misread my paper that they should accuse me not only of ignorance of the distinction between somatic and germinal radiation damage but also of "neglect of elementary methods of critical examination of evidence." My main thesis was that most

for the scientist  
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predictions of the effect of fallout on tumors and life shortening have been based on very scanty evidence and unsupported assumptions. I proposed alternative methods of prediction that use information from animal experiments as well as available human data. I am forced regretfully to conclude that the fallout problem elicits such an emotional response that many otherwise sagacious and objective scientists lose their ability to read accurately and think clearly.

MIRIAM P. FINKEL

Argonne National Laboratory,  
Lemont, Illinois

## Forthcoming Events

### January

12-14. Reliability and Quality Control, 5th natl. symp., Philadelphia, Pa. (W. T. Sumerlin, Philco Corp., 4700 Wissahickon Ave., Philadelphia 44.)

18-31. Bahamas Serendipity Session, Nassau, Bahamas. (B. L. Frank, 1290 Pine Ave., W. Montreal, Canada.)

20-22. American Mathematical Soc., annual winter, Philadelphia, Pa. (E. G. Begle, Leet Oliver Hall, Yale Univ., New Haven, Conn.)

21-22. American Group Psychotherapy Assoc., 3rd annual institute, New York,

N.Y. (C. Beukenkamp, Public Relations Chairman, 993 Park Ave., New York 28, N.Y.)

22-23. Mathematical Assoc. of America, 42nd annual, Philadelphia, Pa. (H. M. Gehman, MAA, Univ. of Buffalo, Buffalo 14, N.Y.)

23-24. American Group Psychotherapy Assoc., 16th annual conf., New York, N.Y. (C. Beukenkamp, Public Relations Chairman, 993 Park Ave., New York 28.)

23-24. Reproductive Physiology and Protein Nutrition, 15th annual conf. on protein metabolism, New Brunswick, N.J. (J. H. Leatham, Rutgers Univ., New Brunswick, N.J.)

24-29. American Acad. of Orthopedic Surgeons, Chicago, Ill. (C. L. Compere, 720 N. Michigan Ave., Chicago, Ill.)

26-29. American Meteorological Soc., New York, N.Y. (K. C. Spengler, AMS, 3 Joy St., Boston 8, Mass.)

26-29. American Soc. of Heating and Air Conditioning Engineers, 65th annual, Philadelphia, Pa. (W. M. Vidulich, ASHACE, 62 Worth St., New York 13.)

26-29. Institute of the Aeronautical Sciences, 27th annual, New York, N.Y. (IAS, 2 E. 64 St., New York 21.)

26-30. Writing and Publication in Industry, conf. and workshops, Brooklyn 1, N.Y. (T. L. Donahue, Writing and Publication Conf., Polytechnic Inst. of Brooklyn, 333 Jay St., Brooklyn 1.)

27-30. Society of Plastics Engineers, Inc., 15th annual tech. conf., New York, N.Y. (L. A. Bernhard, SPE, 65 Prospect St., Stamford, Conn.)

28-29. Nuclear Fuel Elements, 1st intern. symp., New York, N.Y. (H. H. Hausner, 1st Intern. Symp. on Nuclear Fuel Elements, 730 Fifth Ave., New York 19.)

28-31. American Physical Soc., annual, New York, N.Y. (E. R. Fitzgerald, Dept. of Physics, Pennsylvania State Univ., University Park.)

29-31. Western Soc. for Clinical Research, 12th annual, Carmel-by-the-Sea, Calif. (W. N. Valentine, Office of the Secretary, Univ. of California Medical Center, Department of Medicine, Los Angeles 24.)

### February

1-6. American Inst. of Electrical Engineers, winter general, New York N.Y. (N. S. Hibshman, 33 W. 39 St., New York 18.)

3-5. Reinforced Plastics Conf., 14th, Chicago, Ill. (Soc. of Plastics Industry, Inc., 250 Park Ave., New York 17.)

6-7. American College of Radiology, Chicago, Ill. (W. C. Stronach, 20 N. Wacker Dr., Chicago 6.)

9-11. American Acad. of Allergy, Chicago, Ill. (B. Rose, Royal Victoria Hospital, Montreal, P.Q., Canada.)

9-11. Nature of Coal, symp., Bihar, India. (Director, Central Fuel Research Inst., P. O. Fuel Research Inst., Dhanbad District, Bihar.)

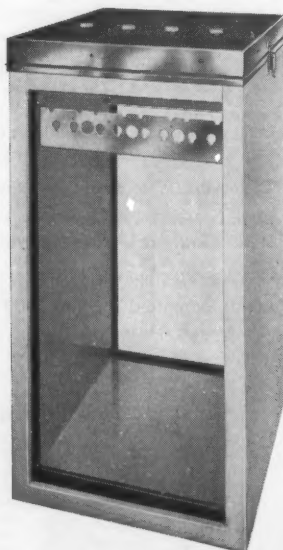
11-13. American Acad. of Occupational Medicine, Boston, Mass. (L. Blaney, 1608 Walnut St., Philadelphia, Pa.)

12-13. Solid State Circuits Conf., Philadelphia, Pa. (A. B. Stern, General Electric Co., Bldg. 3, Syracuse, N.Y.)

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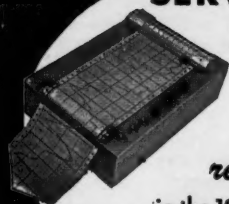
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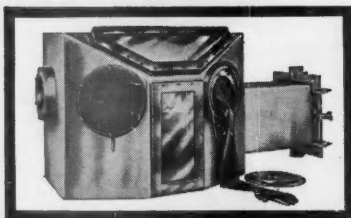
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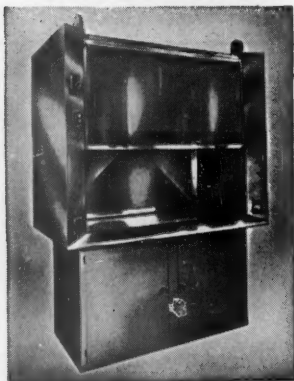
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14. Short Range Navigation Aids., Montreal, Canada. (Intern. Civil Aviation Organization, Maison de l'Aviation Internationale, Montreal.)

15-19. American Inst. of Mining, Metallurgical, and Petroleum Engineers, annual, San Francisco, Calif. (E. O. Kirkendall, AIME, 29 W. 39 St., New York 18.)

16-19. Problems in Field Studies in Mental Disorders, intern. work conf., New York, N.Y. (J. Zubin, American Psychopathological Assoc., 722 W. 168 St., New York 32.)

20-21. Epidemiology in Mental Disorders, annual meeting of the American Psychopathological Assoc., New York, N.Y. (J. Zubin, APA, 722 W. 168 St., New York 32.)

25-26. Midwest Industrial Radioisotopes Conf., Manhattan, Kan. (J. Kitchens, Dept. of Continuing Education, Kansas State College, Manhattan.)

26-28. Genetics and Cancer, 13th annual symp. on fundamental cancer research, Houston, Tex. (Editorial Office, Univ. of Texas, M. D. Anderson Hospital and Tumor Inst. Texas Medical Center, Houston 25.)

27-1. National Wildlife Federation, 23rd annual convention, New York, N.Y. (NWF, 232 Carroll St., NW, Washington 12.)

### March

1-5. Gas Turbine Power Conf., Cincinnati, Ohio. (O. B. Schier, ASME, 29 W. 39 St., New York, N.Y.)

8-9. American Broncho-Esophagological Assoc., Hot Springs, Va. (F. J. Putney, 1712 Locust St., Philadelphia, Pa.)

8-9. American Laryngological Assoc., Hot Springs, Va. (J. H. Maxwell, University Hospital, Ann Arbor, Mich.)

8-12. Aviation Conf., Los Angeles, Calif. (O. B. Schier, ASME, 29 W. 39 St., New York, N.Y.)

10-12. American Laryngological, Rhinological and Otological Soc., Hot Springs, Va. (C. S. Nash, 708 Medical Arts Bldg., Rochester 7, N.Y.)

13-14. American Otological Soc., Hot Springs, Va. (L. R. Boies, University Hospital, Minneapolis 14, Minn.)

15-20. American College of Allergists, San Francisco, Calif. (M. C. Harris, 450 Sutter St., San Francisco.)

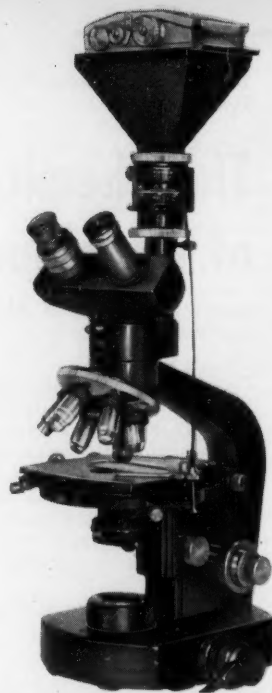
16-20. American Inst. of Chemical Engineers, Atlantic City, N.J. (F. J. Van Antwerpen, AICE, 25 W. 45 St., New York 36.)

16-20. National Assoc. of Corrosion Engineers, 15th annual conf., Chicago, Ill. (NACE, Southern Standard Bldg., Houston, Tex.)

17-19. National Health Council, Chicago, Ill. (P. E. Ryan, 1790 Broadway, New York, 19.)

18-25. International Social Science Council, 4th general assembly (by invitation), Paris, France. (C. Levi-Strauss, Secretary-General, International Social Science Council 19, avenue Kleber, Paris.)

19-21. Society for Research in Child Development, NIH, Bethesda, Md. (Miss N. Bayley, Laboratory of Psychology, National Inst. of Mental Health, Bethesda 14, Md.)



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23-26. Institute of Radio Engineers, natl. conv., New York, N.Y. (G. L. Haller, IRE, 1 E. 79 St., New York 21.)

29-3. Latin American Congress of Chemistry, 7th, Mexico D.F., Mexico.) R. I. Frisbie, Calle Ciprés No. 176, Zone 4, Mexico, D.F.)

30-1. American Orthopsychiatric Assoc., San Francisco, Calif. (M. F. Langer, 1790 Broadway, New York 19.)

30-12. Bahamas Medical Conf., 7th, Nassau. (B. L. Frank, 1290 Pine Ave., W. Montreal, Canada.)

31-2. Symposium on Millimeter Waves, 9th, New York, N.Y. (H. J. Carlin, Microwave Research Inst., 55 Johnson St., Brooklyn 1, N.Y.)

31-5. International Committee of Military Medicine and Pharmacy, 21st session, Paris, France. (Comité International de Médecine et de Pharmacie Militaires, Hôpital Militaire, 79, rue Saint Laurent, Liège, Belgium.)

#### April

1-3. American Assoc. of Anatomists, Seattle, Wash. (B. Flexner, Univ. of Pennsylvania Medical School, Philadelphia 4, Pa.)

1-4. National Council of Teachers of Mathematics, Dallas, Tex. (H. T. Karnes, Dept. of Mathematics, Louisiana State Univ., Baton Rouge 3.)

1-4. National Science Teachers Assoc., 7th natl. conv., Atlantic City, N.J. (R. H. Carlton, NSTA, 1201 16 St., NW, Washington 6.)

1-4. Neurosurgical Soc. of America, Hot Springs, Va. (F. P. Smith, 260 Crittenden Blvd., Rochester 20, N.Y.)

1-29. World Meteorological Organization, 3rd session of congress, Geneva, Switzerland. (WMO, Campagne Rigot, 1, avenue de la Paix, Geneva.)

2-4. Association of American Geographers, 55th annual, Pittsburgh, Pa. (J. E. Guernsey, 9707 Parkwood Dr., Bethesda, Md.)

2-4. Association for Computing Machinery, Cleveland, Ohio. (J. Moshman, Corporation for Economic and Industrial Research, 1200 Jefferson Davis Highway, Arlington 2, Va.)

2-4. Optical Soc. of America, New York, N.Y. (S. S. Ballard, Scripps Institution of Oceanography, Univ. of California, San Diego 52.)

3-4. Eastern Psychological Assoc., Atlantic City, N.J. (C. H. Rush, Standard Oil Co. of New Jersey, Rockefeller Plaza, New York, N.Y.)

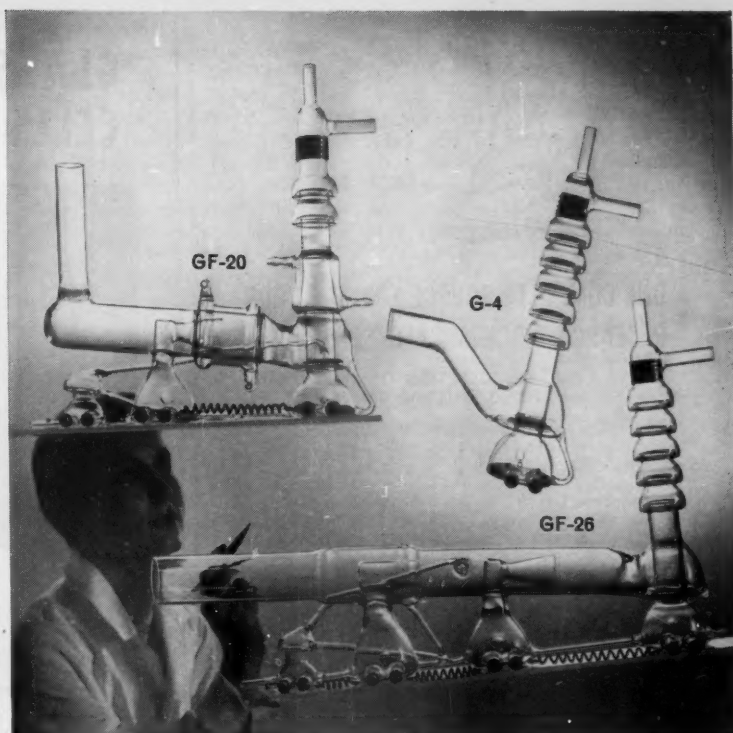
3-5. American Soc. for the Study of Sterility, Atlantic City, N.J. (H. H. Thomas, 920 S. 19 St., Birmingham 5, Ala.)

3-5. Cooper Ornithological Soc., Berkeley, Calif. (J. Davis, Univ. of California, Hastings Reservation, Jamesburg Route, Carmel Valley.)

5-9. American College of Obstetricians and Gynecologists, Atlantic City, N.J. (J. C. Ullery, 15 S. Clark St., Chicago 3, Ill.)

5-10. American Chemical Soc., 135th, Boston, Mass. (M. A. H. Emery, 18th and K St., NW, Washington, D.C.)

5-10. Nuclear Congress, Cleveland, Ohio. (S. Baron, Burns & Roe, Inc., 160 West Broadway, New York 13.)



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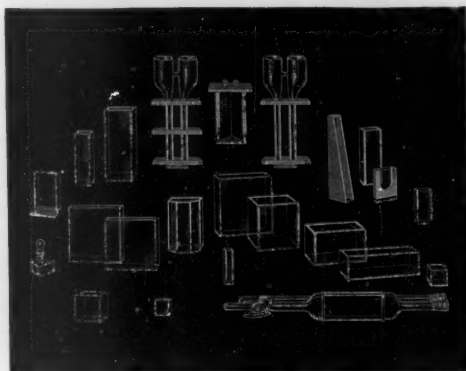
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■ **WATER-FLOW SWITCH** allows water-cooled chemical apparatus to be left unattended in safety. Cooling water flowing through the device produces a hydrostatic head that is used to actuate a diaphragm-type switch. Failure of flow cuts off power to the apparatus and actuates an alarm. A short time delay permits brief interruption of flow for adjustment purposes without actuating the safety device. (Instruments for Research and Industry, Dept. 536)

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■ **TEMPERATURE INDICATOR** uses thermistors to indicate temperature at ten different points to  $\pm 0.1^\circ\text{C}$  accuracy. Range is  $60^\circ$  to  $90^\circ\text{C}$ . Indication is by a meter calibrated in  $0.2^\circ\text{C}$  graduations. Other ranges and coverage of more or fewer than 10 points can be provided. (Fenwal Electronics Inc., Dept. 538)

■ **LABORATORY SINK** is made of  $\frac{3}{8}$ -in. thick, high-temperature, high-density polyethylene. Inside dimensions are 15 by 20 by 8 in. A 1-in. flange surrounds the open top. A  $1\frac{1}{2}$ -in. flanged center sink trap provides drainage. (American Agile Corp., Dept. 541)

■ **SCALE-DRAWING MACHINE** is a hand-operated device that allows the redrawing of any electrical indicating instrument whose angular deflection is not greater than  $90^\circ$ . Thus electrical indication may be returned to original accuracy after repair or calibration. Purchase of the device includes a 40-hour in-plant course of instruction in its operation. (Sensitive Research Instrument Corp., Dept. 543)

■ **WHEATSTONE BRIDGE** features accuracy of  $\pm 0.02$  percent for most measurements from 0 to 12,000 megohm. The lowest range has a resolution of 10  $\mu$ ohm per dial division. The range-switching circuit is designed so that switch contacts never appear in series with a low-resistance bridge arm. A ratio adjustment is provided for each range setting so that each range can be independently adjusted to a known reference standard. The variable resistance arm is a five-place decade rheostat initially adjusted to accuracy of  $\pm 0.005$  percent + one dial division. (Electro Measurements Inc., Dept. 539)

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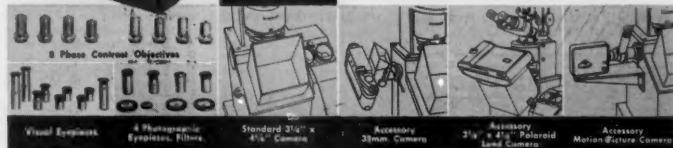
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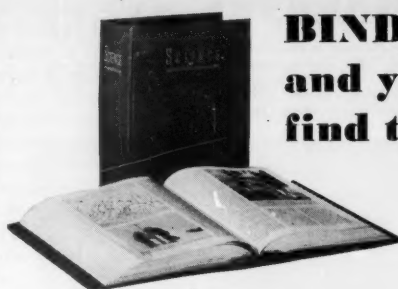
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1/16; 2/20; 3/20; 4/17

(a) Clinical Chemist; M.S., Ph.D. experienced in hormone analysis, toxicology, chromatography; potential department head; research, testing laboratories; to \$10,000; California. (b) Bacteriologist; M.S. preferred; newly created position in central laboratory serving hospitals supervised by three pathologists; research opportunity if desired; to \$6000; resort community fairly near Chicago. (c) Biochemist; M.S., Ph.D. experienced clinical chemistry; newly created position involves complex chemistries, investigative work, supervision of department; 200-bed general hospital; \$7200; Southwestern capital city. (d) Bacteriologist; assist chief bacteriologist with steadily increasing workload; hospital now doubling to 800 beds; minimum \$6000; university city 200,000; Southwest central. Woodward Medical Bureau, Ann Woodward, Director, 185 North Wabash, Chicago. X

### POSITIONS OPEN

Microbiologist-Antibiotics. Eastern pharmaceutical firm has opening for able Ph.D. with laboratory fermentation experience in antibiotic field. Please send résumé of academic training and experience. Box 251, **SCIENCE**. 12/26; 1/2

Nutritional Biochemist. Opportunity for young man to head group in nutritional research. Mainly involves animal nutrition studies with rats and chicks, using biochemical techniques to augment the nutritional data. Qualifications: Ph.D., age 26 to 38, with two to several years of pertinent research experience. Salary dependent upon qualifications. Relocation expenses and attractive benefits. Please reply with a résumé and salary requirement to Professional Employment Manager, Mead Johnson and Company, Evansville 21, Indiana. X

Postdoctoral Traineeships in lipid chemistry are available for 1959 at the University of Tennessee Medical Units, Memphis. The program offers persons holding Ph.D. and M.D. degrees an opportunity to learn modern analytical techniques in lipid chemistry, including the use of radioactive isotopes. Applications may be sent to Dr. D. B. Zilversmit, Department of Physiology. X

Postdoctoral Traineeships in enzyme chemistry are available for 1959-60 at the University of Wisconsin, Institute for Enzyme Research in Madison. Applications may be submitted at any time and are invited from candidates who have completed or who will shortly complete the requirements for either the Ph.D. or M.D. degree. The period of traineeship is 12 months (including 1 month's vacation) and may be renewed for additional years. Stipends are \$6000 per year and in most cases are partially tax-exempt. A travel allowance is provided the trainee from his present institution (if within continental United States) to Madison. Senior traineeships are available to persons who by virtue of previous postdoctoral training and/or experience have demonstrated outstanding ability. Application forms and information may be obtained by writing to Dr. David E. Green, Program Director. 12/19



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## SOUTH AFRICAN COUNCIL FOR SCIENTIFIC AND INDUSTRIAL RESEARCH—RESEARCH OFFICER

Applications are invited for the above-mentioned post in the Amoebiasis Research Unit at the Medical School, University of Natal, Durban, Union of South Africa.

Applicants should have at least an M.S. degree, or its equivalent, preferably majoring in zoology, plus 2 years' appropriate experience. Depending on qualifications and experience, the appointment may be made on one of the following grades:

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Men—£1080 x 60—£1320

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It is obligatory to become a member of the Provident Fund which involves a contribution of 7 percent of basic salary by the Officer and a similar contribution by the Council. The successful applicant will be required to furnish a certificate of good health and chest x-ray examination.

Information regarding general conditions of service may be obtained from the South African Scientific Attaché, 1907 K Street, NW, Washington 6, D.C.

The Council will bear the cost of transfer of the appointee and his family from place of residence to Durban, and will contribute to the cost of transport of household effects.

Applications, giving full details of age, marital status, nationality, scientific and technical qualifications and experience, and the names of at least two persons to whom reference may be made, should be addressed to the Director, Amoebiasis Research Unit, P.O. Box 1035, Durban, Union of South Africa. A copy of the application should be sent to the South African Scientific Attaché, 1907 K Street, NW, Washington 6, D.C. X

## FELLOWSHIPS

The Department of Pharmacology of Cornell University Medical College has instituted a graduate training program in experimental and clinical pharmacology. Tuition fees and stipends are available at the predoctoral and postdoctoral levels for a few suitably prepared candidates. Inquiries should be addressed to Director of Graduate Training, Department of Pharmacology, Cornell University Medical College, 1300 York Avenue, New York 21, New York. X

## SCHOLARSHIPS

### McMASTER UNIVERSITY GRADUATE SCHOLARSHIPS IN BIOLOGY

Applications are invited for graduate research scholarships from qualified students wishing to work toward the M.Sc. and Ph.D. degrees. The stipend for a 12-month period is from \$1700 to \$2200. Research in progress: Ecology, behavior, and nutritional physiology of aquatic and blood-sucking Diptera, emphasizing Simuliids; population dynamics of grasshoppers (D. M. Davies). Sensory physiology and behavior in fish; formation of lake bottom sediments (H. Kleerekoper). Viruses in wild plants; cytological studies (W. D. MacClement). Physiology of sporulation in Ascomycetes; physiology and genetics of yeast (J. J. Miller). Radiobiology and radiation protection; inhalation radiocardiography; cancer transplantation and irradiation; experimental diabetes and beta-cell regeneration; tritium autoradiography (P. F. Nace). Experimental embryogeny; organic terrain organization; palaeobotany and developmental morphology; applied palaeobotany and palynology (N. W. Radforth).

Prospective applicants should write for further information to Professor H. Kleerekoper, Chairman, Department of Biology, Hamilton College, McMaster University, Hamilton, Ontario, Canada. Application forms both for scholarships and graduate study are obtainable from the Dean of Graduate Studies and must be returned to him normally by 1 March 1958, accompanied by university transcript and letters of recommendation from two professors. 12/26; 1/2

## POSITIONS OPEN

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Opportunity available for young physician in Professional Service Department of Medical Division. Should have ability and interest in medical writing. Clinical or laboratory experience desirable. Please send complete résumé to:

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## POSITIONS WANTED

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Parasitologist, Ph.D. June 1958. Desires teaching-research position. Box 253, SCIENCE. X

Scientist with broad experience in teaching and research; Ph.D. biosciences; recently resigned position as director of laboratories, state department of health; experienced in virology, microbiology. Medical Bureau, Burnside Larson, Director, 900 North Michigan Avenue, Chicago. X

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# APPLICATION FOR HOTEL RESERVATIONS

## 125th AAAS MEETING

Washington, D.C., December 26-31, 1958

The list of hotels and their rates and the reservation coupon below are for your convenience in making your hotel room reservation in Washington. Please send your application, *not* to any hotel directly, but to the AAAS Housing Bureau in Washington and thereby avoid delay and confusion. The experienced Housing Bureau will make assignments promptly; a confirmation will be sent you in two weeks or less.

**As in any city, single-bedded rooms at minimum rates may become scarce; double rooms for single occupancy cost more; for a lower rate, share a twin-bedded room with a colleague.** Most hotels will place comfortable rollaway beds in rooms or suites at \$2.00 to \$2.50 per night. Mail your application *now* to secure your first choice of desired accommodations. All requests for reservations must give a definite date and estimated hour of arrival, and also probable date of departure.

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Hotels with an asterisk have sessions in their public rooms. For a list of headquarters of each participating society and section, see page 151, *Science*, July 18.

Hotel	Single	Double Bed	Twin Bed	Suite
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*Shoreham	all 9.00	all 12.00	all 12.00	20.00-50.00
*Statler	all 10.00	all 14.00	all 14.00	24.00-30.00
*Washington	7.00- 8.00	11.00-12.50	11.00-12.50	24.50-45.00
*Willard	10.00-12.50	13.00-17.00	14.00-18.00	25.00-35.00
Roosevelt	7.00- 9.00		10.00-12.00	18.00-24.00
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